Perspective:

A rapidly expanding house of cards: the silent loss of cell physiology hampers marine biosciences

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In the past few decades, the genomic revolution has led to an unprecedented diversification in ecological and evolutionary sciences, enabling astonishing advances. This diversification, however, was not matched with an equivalent increase in faculty positions, leading to the displacement of many sub-disciplines perceived to be less cutting-edge. Similar to the widely recognized waning of taxonomists [1], we perceive a silent and inadvertent loss of cellular biochemists and physiologists in the marine animal science community. Inexorably, this loss in expertise will affect our ability to discover and characterize cellular phenotypes, a task that is essential for understanding the mechanisms that determine responses to ongoing ocean warming, hypoxia, and acidification. Knowledge about cellular and whole-organism biochemistry and physiology is absolutely crucial for characterizing the functions of genes that are under selection by climate change stressors. But while much current research attempts to identify such beneficial standing genetic variation that may help marine animals adapt to rapidly changing oceans [2], the underlying cellular phenotypes remain poorly understood. In addition, biomedical research is uncovering a surprising lack of correlation between gene expression and cell function [3], which highlights the urgent need for a comprehensive understanding of biological processes that extends beyond genomics and transcriptomics.

Cells contain a dense mix of ions, proteins and other organic molecules (e.g. osmolytes) that create a gel-like fluid that fundamentally determines protein and organelle function [4]; the properties of this fluid can greatly vary in organelle-, cell type-and species-specific manners [5, 6]. Although invertebrates constitute ca. 75% of marine animal species [7], there is not a single invertebrate species for which intracellular osmolyte concentrations, acid-base parameters, and carbonate chemistry [5] have been fully characterized. Indeed, the most comprehensive (yet incomplete) assessment of intracellular osmolyte budgets in invertebrates was published >60 years ago [8]. Similarly, detailed information about intracellular acid-base parameters in invertebrates is available from one study only [9]. Unfortunately, this information cannot be obtained from genomic and transcriptomic surveys, yet it is essential for determining the effects of elevated carbon dioxide levels in the ocean as virtually every enzyme is either directly impacted by pH, or post-translationally regulated via acid-base-dependent signaling pathways [10]. Numerous other critical biochemical and cellular processes are surprisingly understudied, including aerobic and anaerobic ATP production, antioxidant responses, biomineralization, and metabolic exchange between symbiotic partners. As a result, and inadvertently, we lack a solid foundation to answer pressing questions in ecology and evolution. How can we assess effects of environmental stressors based on changes in gene expression when we do not know the identity of the relevant genes, or the most basic properties and functions of their coded proteins? How can we test effects of amino acid substitutions on enzyme function when we lack knowledge to design buffers to mimic cellular conditions for *in vitro* assays?

Unfortunately, the field of biochemistry and physiology of marine animals has intrinsic limitations that conspire against its progress and impact. Chief among them, method development is very time-consuming and often results in protocols that can only be performed in specialized laboratories leading to relatively modest publication and citation rates. In the current hyper-competitive academic environment, this combination can discourage junior researchers and be detrimental to early career faculty. In addition, the small and decreasing size of the scientific community in this field constitutes a major hurdle during the review process. Indeed, it is increasingly difficult to find actual peers who can fairly assess the quality of work while also avoiding conflicts of interest. As a result, work is often reviewed by colleagues and editors who lack the required expertise and have other scientific interests, and thus tend to perceive research on biochemistry and physiology as “too specialized”. This generates an unfortunate cycle whereby studies are seldomly published in high profile multidisciplinary journals, affecting the ability of researchers in this field to influence the scientific community, secure funding and faculty positions. Furthermore, the retiring of each colleague results in the loss of an academic role model, completing a ‘vicious’ cycle.

Retirement of colleagues also leads to loss of methodological know-how that, eventually, will have to be re-developed when cellular phenotyping -in the broadest sense- inevitably becomes essential. In the short-term, the theoretical and practical know-how can be preserved through detailed video and written methods and review papers. Ultimately, expert scientists will be needed to identify original questions, develop new methods, interpret results, and promote and generate excitement amongst students and the upcoming generations of scientists. We thus implore research institutions to value and promote the hiring of faculty in the fields of marine biochemistry and physiology. Cluster faculty hires that ‘pair’ them with evolutionary ecologists seem a promising way forward, especially if these work with similar taxa and environments. Only with a strong community of biochemists and physiologists will be able to understand how marine animal species ‘work’, how cellular attributes differ from those of biomedical model organisms, and why some genotypes fare better than others in rapidly changing ocean environments.

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