BRINGING DISCIPLINES AND PEOPLE TOGETHER TO CHARACTERIZE THE PLASTIC AND GENETIC RESPONSES OF MOLLUSCS TO ENVIRONMENTAL CHANGE

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RUNNING HEAD: MOLLUSCS AND ENVIRONMENTAL CHANGE

ABSTRACT

Mollusks are remarkably diverse and are found across nearly all ecosystems, meaning that members of this ancient animal phylum provide a powerful means to study genomic-phenotype connections in a climate change framework. Recent advances in genomic sequencing technologies and genome assembly approaches finally allow the relatively cheap and tractable assembly of high-quality mollusk genome resources. After a brief review of these issues and advances, we use a case-study approach to provide some concrete examples of phenotypic plasticity and genomic adaptation in mollusks in response to environmental factors expected to be influenced by climate change. Our goal is to use mollusks as a "common currency" to demonstrate how organismal and evolutionary biologists can use natural systems to make phenotype-genotype connections in the context of changing environments. In parallel, we emphasize the critical need to collaborate and integrate findings across taxa and disciplines in order to use new data and information to advance our understanding of mollusk biology in the context of global environmental change. We end with a brief synthetic summary of the papers inspired by the 2021 SICB

Symposium “Genomic Perspectives in Comparative Physiology of Molluscs: Integration across Disciplines”.

INTRODUCTION

Mollusca is the second largest Metazoa phylum, representing over 90,000 extant taxa (Rosenberg 2014). Mollusks are found in nearly all aquatic, marine, and terrestrial habitats and harbor remarkable diversity, from octopi, snails, and oysters to the superficially wormlike Aplacophora and Polyplacophora. Originating over 500 million years ago in the Cambrian, mollusks play important ecological, economic, and medical roles across the globe (Rosenberg 2014; Fortunato 2015). Mollusks act as ecosystem engineers by introducing complexity and heterogeneity into their environments, cycling and storing carbon and nutrients, acting as biological filters in estuaries, and stabilizing the shoreline (Coen and Grizzle 2007; Commito 2008). Mollusks also process and sequester calcium in their shells, bringing about habitat transformation by affecting population-, community- and ecosystem-level processes. The bodies and shells of mollusks provide habitat structure and food resources and modify abiotic conditions (Coen and Grizzle 2007; Commito 2008). Mollusk shells can also persist centuries or more after the mollusk itself has died, producing long lasting eco-historical legacies (Schöne and Surge 2005; Fortunato 2015).

Throughout human history, mollusks have served as a food source and were used across cultures and socio-economic contexts for tools, decoration, the souvenir industry, and currency exchange (Maurer 2006; Çakirlar 2011). Many mollusk species are cultivated and harvested, constituting up to 58.8% of the combined production of aquaculture and ca. 7% of capture fisheries worldwide (Darrigran et al. 2020; Dölle and Kurzmann 2020). Some mollusks (e.g., sea hare, *Aplysia*) are used in biomedical research, while others are important agricultural pests (e.g., giant African snail, *Achatina fulica*), invasive species (e.g., zebra mussel, *Dreissena polymorpha*), or intermediate vectors of deadly human parasites (e.g., bloodfluke planorb, *Biomphalaria glabrata*) (Bridger et al. 2018; Guo et al. 2019; Dölle and Kurzmann 2020).

Mollusks have gained recent attention as model species for climate change research. Global climate change is proceeding at an unprecedented rate, with major consequences for all ecosystems. A critical question in this setting whether and how natural populations will respond to global climate change and if these responses will be rapid and adequate enough for species persistence. In general, populations respond to environmental change by one or a combination of four strategies (1) shifting their range, (2) phenotypic plasticity, (3) genetic adaptation via evolution by natural selection to new conditions, and (4) persisting in the original habitat but experiencing demographic decline or extinction (Waldvogel et al. 2020).

Their high diversity and abundance along with presence across wide latitudinal clines and preservation in the fossil record means that mollusks can serve as a powerful indicator of environmental changes in all ecosystems (Fortunato 2015). Mollusks as recorders of environmental proxies are already providing valuable information about global change in aquatic ecosystems that is facilitating conservation strategies. For example, the ‘Mussel Watch Program’, created by NOAA’s National Centers for Coastal Ocean Science (NCCOS) in response to concerns over environmental quality of the coastal and estuarine ecosystems, is one of the most successful continuous chemical contaminant biomonitoring program in the U.S. (Kimbrough et al. 2008).

In the following sections, we will use a case-study approach to provide some concrete examples of phenotypic plasticity and genetic adaptation in mollusks in response to global change (Fig. 1). Our survey is by no means exhaustive. Instead, our is goal is to introduce organismal and evolutionary biologists to questions of processes and patterns of organismal change, using mollusks as a “common currency”. We also discuss the need to collaborate and integrate findings across multiple disciples in order to leverage the recent availability of new DNA sequencing technologies and big genomic datasets to advance our understanding of mollusk biology in the context of global environmental change. We conclude by providing a synthesis of discussions held during the 2021 SICB Symposium “Genomic Perspectives in Comparative Physiology of Mollusks: Integration across Disciplines” alongside a summary of invited papers in this special issue.

MOLLUSCAN RESPONSES TO ENVIRONMENTAL CHANGE:

As is all too common in mollusks, we know comparatively little about phenotypic plasticity and genetic variation and its association - or lack thereof - with phenotypes associated with environmental stress. Most of what we do know has come from a handful of taxa that receive relatively focused attention as model organisms. We here highlight a diverse set of Molluscan taxa that provide illustrative examples of response to various environmental stresses. It is important to note that we were unable to find a substantial body of directly relevant data (i.e., evidence for intraspecific genetic variation and/or phenotypic plasticity corresponding to differential phenotypic responses to environmental stresses) from the Molluscan classes Scaphopoda, Monoplacophora, Aplacophora, or Polyplacophora (also see Yang et al. 2020; Davison and Neiman 2021), highlighting that there is still a great deal of work left to do. Nevertheless, we believe that this overview will provide a useful starting point with respect to assessing the potential for adaptive change in mollusks in a rapidly changing world.

1) Phenotypic Plasticity:

Phenotypic plasticity is defined as a situation when a genotype produces different phenotypes in response to different environmental conditions. Phenotypic plasticity is ubiquitous, and most traits are plastic (reviewed in Ghalambor et al. 2007). Ghalambor et al. (2007)'s review also described a wide range of consequences of plasticity with regard to organismal fitness, which in turn is a function of the particular environmental changes and the physiological limits of the organisms involved.

The specific way in which a particular genotype responds to different environments is described as a reaction norm, which can be represented by continuous or discrete character states depending on the type of trait involved (Woltereck 1909; Falconer 1990, Ghalambor et al. 2007). With respect to global change, reaction norms provide information on extant levels of phenotypic plasticity and the potential sensitivity of organisms to future global change scenarios including shifts in ecological niche breadth and resource management strategies (Ghalambor et al. 2007, 2015). Studies on phenotypic plasticity in mollusks can provide useful and actionable information regarding climate change by integrating -omic approaches. For examples, genomics-enabled studies of phenotypic plasticity can provide information about relevant genetic loci as well as transcripts that are regulated with high sensitivity for determination of physiological state (e.g., energetics, stress) and plasticity in response to environmental factors affected by climate change (e.g., pH, temperature, hypoxia) (Stillman and Armstrong 2015).

a) Case study 1:

Gastropods. Nudibranchs: indicator species for tolerance–plasticity trade-off hypothesis of thermal tolerance?

Nudibranchs are soft-bodied intertidal eurythermal marine gastropods that have neither an external shell nor a water-impermeable cuticle. The absence of a shell/cuticle – in contrast to most other mollusks – and their limited mobility makes nudibranchs especially sensitive to their environment. Nudibranchs are thus particularly useful “indicator species” to study traits like thermal plasticity (Goddard et al. 2011; Nimbs et al. 2016; Sanford et al. 2019). A good example is provided by Armstrong et al. (2020), who investigated thermal plasticity including heat tolerance limits (CT_{max}) and plasticity, temperature sensitivity of metabolism, and metabolic cost of heat shock in nine species of nudibranchs collected across a thermal gradient along the northeastern Pacific coast of California. The authors reported that adaptation to relatively warm water temperatures in intertidal nudibranchs constrains plasticity to acute thermal challenge and that southern (warm adapted) species are likely most vulnerable to future warming. Climate-related range expansions were reported during relatively warm periods (between 2014 and 2017) in more than 52 eastern Pacific nudibranch species (Goddard et al. 2018). In the southern hemisphere, an inverse southward expansion (from tropical to subtropical waters) has been reported in four tropical species of nudibranch along the Australian coast (Nimbs et al. 2015, 2016). These studies show that heat tolerance plasticity is strongly and negatively correlated with inherent heat tolerance in nudibranch mollusks. These findings are broadly in accordance with the trade-off hypothesis of thermal adaptation (Stillman 2003), which posits that organisms already adapted to high temperatures have limited scope to further increase their heat tolerance via phenotypic plasticity.

b) Case study 2:

Bivalves. Oysters: strong cellular homeostasis system is a unique adaptive characteristic

The oyster is a major aquaculture species worldwide, with the highest annual production of any marine organism (http://www.fao.org). Oysters are champions of survival in the face of harsh and dynamically changing environments in estuarine and coastal zones. These habitats experience wide temporal and spatial fluctuations of temperature and salinity, and desiccation presents a serious challenge during daily and seasonal cycles. As reviewed in Zhang et al. (2016), oysters are eurythermal (range from below 0°C to 49°C), euryhaline (salinity tolerance below 10 parts per thousand and in excess of 35 parts per thousand), and have substantial tolerance to hypoxia and anoxia. Oysters also withstand high levels of pollutants, can concentrate metals to levels 10^3- to 10^6-fold higher than those of the surrounding water, and are regarded as the most useful model for studying chemical pollution in aquatic environments (reviewed in Zhang et al. 2016). Oysters have evolved remarkable phenotypic plasticity in the face of this environmental stochasticity, making these bivalves a uniquely powerful model for the study of physiological mechanisms of stress tolerance and adaptation.

Oysters have developed a wide range of sophisticated response mechanisms to maintain cellular homeostasis under stress, revealed through physiological studies (e.g., Zhang et al. 2016) and functional genomic and molecular approaches (e.g., Zhang et al. 2012). A robust homeostasis system that includes chaperone-dominated protein folding systems (HSPs and three UPR signaling pathways), xenobiotic biotransformation systems (YP450 and flavin-containing monooxygenase, glutathione S-transferases, and ATP binding cassette (ABC) transporters), and a complex antioxidant system of enzymes enables oysters to exhibit remarkable phenotypic plasticity under stress conditions (e.g., Schlenk and Buhler 1989; Boutet et al 2004; Kingtong et al 2007; Fabbri et al 2008; Limon-Pacheco et al 2009; Zanette et al 2011; Zhang et al 2012; reviewed in Zhang et al. 2016). The oyster genome and transcriptome have provided a global view of the complex defense system via analysis of genome structure, gene evolution, and defenses under different stressors (Zhang et al. 2012). The expansion of key defense gene families and the strong transcriptomic response to stress highlight sophisticated genomic adaptations to sessile life in a highly stressful environment (Zhang et al. 2015).

c) Case Study 3:

Cephalopods. Squids: champions of hypoxia survival

Cephalopods are one of the most adaptable marine organisms, featuring a wide range of life history plasticity driven by variation in environmental conditions (Boyle and Rodhouse 2005; Hoving et al. 2013). For example, some squid taxa (e.g., Ommastrephidae) occupy oceanic niches characterized by relatively low oxygen saturation, display remarkable extremes of phenotypic plasticity, and have evolved novel physiological strategies to survive in their habitats (Seibel 2016). These species both illuminate the mechanistic process of biological regulation and forecast possible responses of marine animals to future climate change. In the last few decades, marine hypoxia has become a major ecological concern (Diaz & Rosenberg, 2008). Naturally occurring oxygen minimum zones (OMZs) with <20 μM oxygen (<10% of air saturation) constitute nearly 10% of the global ocean's volume (Paulmier and Ruiz-Pino 2009). The synergistic impact of climate-related drivers like global warming and ocean acidification further reduces oxygen availability, thereby shifting, narrowing, and compressing habitable depth and geographical ranges for many taxa (Seibel 2016).

Some squid taxa that were expected to be driven out of hypoxic areas as a consequence of anatomical and physiological constraints (e.g. *Dosidicus gigas*) instead seem to benefit from expanding hypoxia (Rosa and Seibel 2010). These squid manage to thrive under such conditions by maximizing oxygen extraction capabilities for aerobic survival in the upper ocean and by undergoing metabolic suppression during oxygen limitation at depth during the daytime (Seibel et al. 2014). In *D. gigas*, the oxygen consumption rate under 1% oxygen (P_{O2} of ∼1.0 kPa) is only ∼20% of the control rate (Rosa and Seibel 2008, 2010; Seibel et al. 2014) and metabolism (including both aerobic and anaerobic energy sources) is suppressed by ∼50% relative to controls. The remaining energy that the squid needs to thrive is generated by the activation of plastic pathways including anaerobic glycolysis and anaerobic mitochondrial metabolism that are only turned on under hypoxic conditions (Seibel 2016). Further research characterizing the molecular mechanisms facilitating this metabolic flexibility will provide an important step forward. In addition to global metabolic depression, plasticity at the transcriptional level turns on a number of hypoxia-inducible microRNAs (Hadj-Moussa et al. 2018). These microRNAs are potentially involved in cytoprotective mechanisms including neuroprotection, anti-apoptosis, regenerative mechanisms in the brain, and inhibition of apoptosis and cell proliferation, while conserving energy in the heart and limiting damage by reactive oxygen species and apoptosis in muscle (Hadj-Moussa et al. 2018).

2) Genetic Adaptation:

Genetically based responses are the most relevant and powerful driver of long-term adaptive responses to climate change. Genomic data provides direct insight in the genetic underpinnings of these responses and is thus a central element of deciphering the mechanisms driving evolutionary adaptation to climate change (Gienapp et al. 2008; Merilä 2012).

Investigating genetic adaptation under changing environmental conditions requires knowledge of the initial (ancestral) genetic state as well as the adapted/evolved state in the new conditions (Waldvogel et al. 2020). There are two approaches commonly used to characterize the ancestral state: 1) space-for-time approach (the initial state is correlated to environmental and/or genetic heterogeneity) and 2) time-for-space approach (initial state is tracked through evolutionary time). Both of these approaches provide critical information: the former with respect to standing genetic variation, and the latter the likelihood of the evolutionary change from the known ancestral state (see Waldvogel et al. 2020 for details).

Understanding whether and how organismal populations can adapt to changing environmental conditions requires characterization of intraspecific genetic variation underlying organismal phenotypic variation in relevant environments because this variation provides the raw material for evolution by natural selection (Lewontin 1974). To what extent does genetic variation for phenotypic responses to environmental stressors exist within natural mollusk populations? This question is of critical importance both with respect to the aquaculture industry (Bernatchez et al. 2017), which plays a central role in meeting current and future food needs (Béné et al. 2016; Food and Agriculture Organization of the United Nations 2016), and in terms of predicting whether mollusk populations will be able to adapt to anthropogenic change. Broad statements regarding the genesis of intraspecific adaptive genetic diversity in mollusks will require comprehensive study of multiple members of all Mollusca classes. While inferences are limited by the narrow phylogenetic scope of available data, there is a growing body of evidence suggesting that at least some mollusk taxa feature notably high intraspecific structural variation that could in turn be adaptive (e.g., Zhang et al. 2012; Gerdol et al. 2020; Rogers et al. 2021; McElroy et al. in review).

It is less clear that nucleotide substitution will typically underlie evolutionary adaptation to environmental stresses in mollusks. While we again are limited to very cautious statements in light of the phylogenetically limited scope of relevant data, genomic data from bivalves like scallop (Wang et al. 2017) and mussel (Rogers et al. 2021) hint that structural changes like gene family expansion might ultimately be a more important source of adaptive change than single-nucleotide polymorphism at least in some taxa. Future studies should address genotype-phenotype relationships with respect to intraspecific structural polymorphisms, especially for the expanded gene families that seem to hold particular potential in contributing to stress-related adaptions in mollusks (e.g., Zhang et al. 2012, 2016; Sun et al. 2017; reviewed in Yang et al. 2020).

d) Case Study 4:

Gastropods. Potamopyrgus antipodarum - *from pristine New Zealand lakes to invasion worldwide.*

These tiny New Zealand freshwater snails have risen to prominence as a model system both because of the unusual coexistence of obligately sexual and obligately asexual individuals within populations (Lively 1987) and because they are global invaders of aquatic ecosystems (Alonso and Castro-Díaz 2012). The ability to culture genetically distinct asexual lineages in the laboratory makes *P. antipodarum* an especially powerful model system with respect to identifying genetic variation for various phenotypic traits (e.g., Song et al. 2021), though the next steps of characterizing the genetic basis for this variation is much more difficult in an asexual setting.

To date, evidence for genetic variation for response to environmental stressors in *P. antipodarum* has come from studies of host-parasite interactions (e.g., Dybdahl and Lively 1995, 1998), salinity (Jacobsen and Forbes 1997), nutrient limitation (Neiman et al. 2013; Neiman and Krist 2016), temperature (Dybdahl and Kane 2005; Sharbrough et al. 2017), flow rate (Kistner and Dybdahl 2013), predation (Levri et al. 2017), and cadmium exposure (Jensen et al. 2001). These data do suggest that *P. antipodarum* can exhibit adaptive evolutionary responses to changing environments, though Verhaegen et al. (2018) suggested that a fairly minimal contribution of genetic background vs. plasticity to adaption to flow rate emphasizes plasticity over genetic variation as a potential driver of the widespread invasion of *P. antipodarum.*

e) Case Study 5:

Bivalves. Mytilus spp.: Can aquacultured organisms survive - *and even thrive during* - *climate change?*

These primarily saltwater mussels are found around much of the world and are of wide interest as an edible and readily aquacultured group. From a biological standpoint, various *Mytilus* taxa have risen to prominence as models for mitochondrial biology (e.g., Hoeh et al. 1991; Quesada et al. 1998; Ladoukakis and Zouros 2001; recently reviewed in Zouros and Rodakis 2019), as subject to contagious cancers (Metzger et al. 2016; Yonemitsu et al. 2019), and for elucidating the mechanisms underlying adaptation to temperature regime (e.g., Hilbish et al. 1994; Lockwood et al. 2012).

As early as 1977, researchers demonstrated that *Mytilus edulis* exhibited genetic variation for responses to salinity (Innes and Haley 1977). Similar results with respect to salinity were subsequently reported by, for example, Bulnheim and Gosling (1988). In 2006, Freeman and Byers showed evidence consistent with a scenario whereby *M. edulis* harbors genetic variation for adaptive anti-predator responses to an invasive crab. More recent studies involving *M. edulis* have demonstrated standing adaptive genetic variation with respect to recently reported spring mortality outbreaks of unclear origin

(Dégremont et al. 2019) and stresses imposed by ocean acidification (Bitter et al. 2019), and hinted that pollution might also drive adaptation (Larsson et al. 2016). In the congener *M. galloprovicialis*, Han and Dong (2020) used whole-genome sequencing data to identify adaptive genetic variation associated with environmental variables linked to heat stress. Altogether, the picture appears positive with respect to the future, though it seems imperative that aquaculturists include careful consideration of heritable variation for adaptive responses to expected environmental stresses when choosing breeding and culture stock.

f) Case Study 6:

Cephalopods: Does ecological opportunism and RNA editing drive recent proliferation?

Cephalopods are of wide economic and scientific interest because this ancient lineage of mollusks are often keystone species, have independently evolved sophisticated cognitive abilities, and are an important food source across the globe. Even so, no cephalopod taxon has emerged as a focus of study connecting genetic variation to phenotypes relevant to climate change. The absence of such a cephalopod model for evolutionary response to climate change might be linked to widespread challenges associated with laboratory culture, the difficulty of studying deep-water taxa, their large and often highly repetitive genomes, and the hundreds of millions of years separating cephalopods from other, better characterized animal taxa (Xavier et al. 2015; O'Brien et al. 2018; Uriarte et al. 2019).

Nevertheless, Xavier et al. (2014) argue that the persistence of coleoid cephalopods through multiple major extinction events and, more recently, surviving and even thriving despite competition with fish, has preadapted cephalopods to effectively respond to changing environments. An analogous argument was posed by Doubleday et al. (2016), who hypothesized that there might be a connection between the recent striking global increases in the abundance of many cephalopod taxa, and global climate change. O'Brien et al. (2018) took this hypothesis a step further by suggesting that the remarkably extensive RNA editing discovered in cephalopods might contribute to this phenomenon. Whether these hypotheses will be supported will become clear in decades to come as climate change proceeds.

WHY A SYMPOSIUM ON MOLLUSCS: INTEGRATION ACROSS DISCIPLINES?

The revolution in DNA sequencing technologies has translated into the generation of huge bodies of data along with new genomes assembly approaches. Together, these new technologies and analytical approaches are finally allowing for the production of high-quality molluscan genome assemblies. Genome sequence data provide a particularly powerful means of linking genotype and phenotype with respect to molluscan responses (phenotypic plasticity and/adaptation) to global change. Genomic approaches can also help dissect mechanistic underpinnings by which adaptation to climate change occurs (e.g., inherited gene regulation differences by epigenetic mechanisms such as DNA methylation or histone modification; Bossdorf et al. 2008; Franks and Hoffmann 2012; via fixation of specific alleles during adaptive shifts; Hohenlohe et al. 2010).

A mechanistic understanding of the genetic basis of organismal physiology is a critically important element of forecasting whether and how organisms will respond to rapidly changing environments, which represents an urgent challenge for biologists. Our symposium used mollusks as a common currency to link biologists in otherwise quite disparate fields (e.g., biomedicine, physiology, ecology) to address genome-to-phenome research.

Newly developed genomic technologies and bioinformatic approaches have opened up new opportunities for biologists to address questions of both processes and patterns of organismal change. How can we understand the functional context of such “big” data within the intact organism, and how does genomic variation contribute to phenotype? Our symposium is especially novel from the perspective of bringing together the organismal biologists, ecophysiologists, and genomicists/bioinformaticians that are needed to provide a qualitative step forward in understanding the biology and ecology and predicting the future of one of the most important animal groups alive today. Presentations, discussions, and syntheses focused on topics including overviews of the biological and genomic diversity of molluscan life, technological progress towards highly contiguous molluscan genomes, challenges in assembling molluscan genomes, and how genome-scale processes underpin organismal physiology and interact with ecological and evolutionary processes over multiple spatiotemporal scales can be found throughout the special issue that our symposium inspired.

SYNTHESIS OF SYMPOSIUM PAPERS

This special issue presents a series of papers addressing mollusk genome-to-phenome responses in the context of global climate change. Connecting genotypes and genomic variation to functional and ecological consequences demands tools and concepts from a diverse set of fields including molecular biology, physiology, quantitative genetics, ecology, and evolutionary biology. This type of integrated approach will help to identify and decouple genetic vs. plastic underpinnings of ecologically relevant functional variation and characterize the ecological consequences of that variation. Our goal for the symposium was to bring together a transdisciplinary set of experts in mollusk biology to provide an unprecedented opportunity for knowledge exchange, discussion, and catalysis of new partnerships. The talks in our symposium featured a wide range of ecologically important concepts and traits including but not limited to immune function and symbiosis to mitochondrial performance and host-parasite interactions, and are united by their use or application of genomic techniques and resources.

Ghiselli et al. provide a comprehensive review of one of most striking features of bivalve mollusks: their peculiar mitochondrial genome biology. As Ghiselli et al. describe, bivalves have facultatively anaerobic mitochondria that allow them to survive prolonged periods of anoxia/hypoxia. Mollusks also exhibit the only known and evolutionarily stable exception to the strictly maternal inheritance of mitochondria, so-called doubly uniparental inheritance, now described in 100+ molluscan taxa to date. In this review, the authors highlight recent works studying mitochondrial biology in bivalves at the genomic and physiological level and stress that an integrated approach and collaborative relationships are the only possible ways to succeed in connecting mitochondrial genome-to-phenome relationships in bivalves.

Griffiths et al. used a single-generation selection experiment and pooled sequencing of larvae from the eastern oyster (*Crassostrea virginica*) to identify adaptive genetic variation for tolerance to low salinity in two populations from the Gulf of Mexico. The authors compared allele frequencies at 152 salinity-associated genes for larval families pre- and post-low salinity exposure and used these data to demonstrate evidence for purging of deleterious alleles at the larval stage in *C. virginica*. This study also revealed standing genetic variation for salinity tolerance and demonstrated increases in allele frequencies at multiple loci following selection, indicating a polygenic basis for adaptive responses to low salinity but also suggesting that some components of tolerance are genotype specific.

Tanner et al. measured thermal plasticity in two central California eelgrass sea hare (*Phyllaplysia taylori*) populations under four temperature-salinity scenarios in a laboratory acclimation experiment. Acclimation to warmer conditions significantly increased critical thermal minima, while low-salinity conditions resulted in high mortality. Individuals that survived the low-salinity treatments were able to respond to temperature and salinity stresses more rapidly than individuals acclimatized to saltier conditions, though the most rapid response time for the low-salinity acclimatized sea hares was at a higher temperature than the individuals acclimatized to saltier conditions. Together, these results led the authors to conclude that acclimation to climate change-induced warming will likely present challenges with respect to the ability of these sea hares to weather existing and predicted cold extremes and precipitation events.

Furr et al. explored genetic structure and physiological responses to hypoxia and immune stress challenge (the pathogen *Vibrio vulnificus*) across four populations of *Crassostrea virginica* along the North Carolina and Virginia coast. The authors observed significant genetic structure with respect to the distribution of mitochondrial cytochrome oxidase subunit I (COI) haplotypes between locations. The expression of stress-response genes including toll-like receptors, mannose receptor, defensin, and the complement gene Cq3 was specific to locations as well as to the stressors involved. Altogether, these data hint at a complex relationship between genotypes, phenotypes, and stress responses, with indirect evidence for both plasticity and genetic variation for stress responses.

Heath-Heckman and Nishiguchi used newly generated genomic sequence data from four bobtail squid taxa (*Euprymna hyllebergi*, *Euprymna albatrossae*, *Rondeletiola minor*, *Sepietta neglecta*), to identify regions of the genome in bobtail squids that are under selection in squid lineages that maintain symbioses with bioluminescent bacteria (all but *S. neglecta*), setting the stage to identify genes instrumental in the evolution of these mutualistic associations. This study also provided new genomic resources that will be useful for comparative work in cephalopods and beyond.

SUMMARY & CONCLUSIONS

Our symposium and symposium papers illuminate the power and utility of mollusks as model organisms in a variety of contexts and how organismal and evolutionary biologists can leverage these fascinating organisms to generate new insights into phenotype-genotype connections. These connections are especially relevant and important in the context of anthropogenic change. We believe that we have made a strong case that mollusks can be applied to characterize the potential of and limits to plastic and evolutionary change in response to these planetary consequences of human activities. We also have emphasized the central role that cross-disciplinary collaboration and integration will play in the achievement of these goals.

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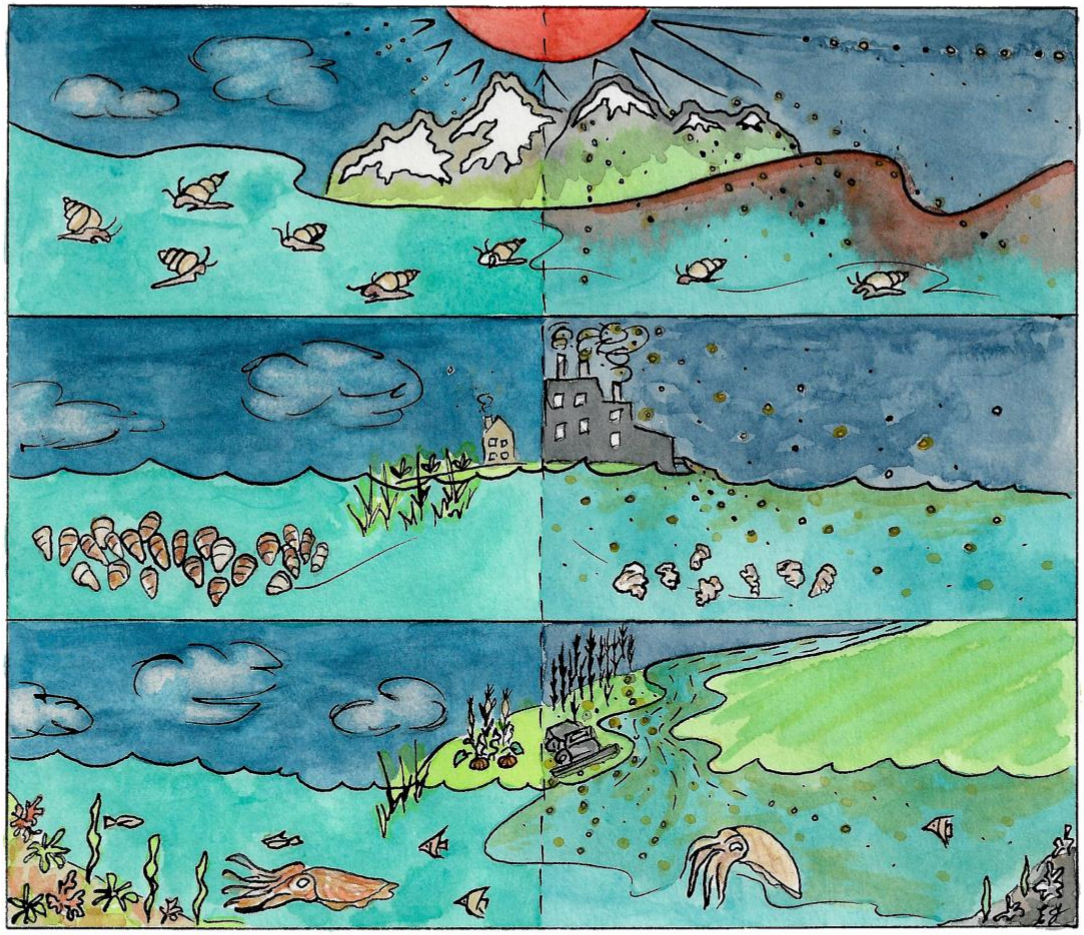

FIGURE LEGEND.

Figure 1. Three examples of stressors that mollusks experience as consequence of anthropogenic changes: rising temperatures (top panel), ocean acidification (middle panel), and hypoxic zones (bottom panel). Art by Emily Jalinsky.

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