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Perspective

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Characterizing the multivariate physiogenomic response to environmental change

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Global change is altering the climate that species have historically adapted to – in some cases at a pace not recently experienced in their evolutionary history – with cascading effects on all taxa. A central aim in global change biology is to understand how specific populations may be "primed" for global change, either through acclimation or adaptive standing genetic variation. It is therefore an important goal to link physiological measurements to the degree of stress a population experiences (*Annual Review of Marine Science*, 2012, 4, 39). Although "omic" approaches such as gene expression are often used as a proxy for the amount of stress experienced, we still have a poor understanding of how gene expression affects ecologically and physiologically relevant traits in non-model organisms. In a From the Cover paper in this issue of *Molecular Ecology*, Griffiths, Pan and Kelley (*Molecular Ecology*, 2019, 28) link gene expression to physiological traits in a temperate marine coral. They discover population-specific responses to ocean acidification for two populations that originated from locations with different histories of exposure to acidification. By integrating physiological and gene expression data, they were able to elucidate the mechanisms that explain these population-specific responses. Their results give insight into the physiogenomic feedbacks that may prime organisms or make them unfit for ocean global change.

KEYWORDS
adaptation, climate change, ecological genetics, transcriptomics

A key question in global change biology today is whether species will be able to keep up with rapid environmental change. As anthropogenic carbon dioxide diffuses into the coastal oceans, it shifts the balance of ions. Hydrogen ions increase, resulting in a decline in pH (acidification), and carbonate ions decrease, making it harder for organisms like corals and molluscs to make their skeletons or shells. As a result, marine ecosystems worldwide are threatened by an anticipated pH drop of 0.3–0.7 units over the next century, a rate of change that is without precedent for marine species in their recent evolutionary history (Caldeira & Wickett, 2003). Although there are many pieces to understanding if species will keep up with this rapid change, the role of standing genetic variation has received a considerable amount of attention because the probability of evolutionary rescue from new mutation is low (Barrett & Schluter, 2008).

As a reasonable starting point to quantify standing genetic variation to ocean acidification, Griffiths, Pan, and Kelley (2019) use data on the pH seascape across the range of a temperate coral (Figure 1a) to identify two populations that have been exposed to different extremes of pH conditions. The first population comes from a location that experiences lower pH due to a high degree of upwelling. Upwelling is an oceanographic process that delivers cold, deep water to the coastline; this water is more acidic because of the pressure and temperature of the water at depth. Griffiths et al. (2019) compare this "high upwelling" (HU) population to a "low upwelling" (LU) population that had historically experienced less acidic, higher pH

conditions. This comparison can give insight into whether the HU population possesses special qualities that will prime it for future ocean conditions.

While quantifying population-specific responses to stress is a key piece to predicting how species will respond to climate change, this can actually be quite challenging to quantify because it can be measured in so many different ways. To provide a more complete picture, Griffiths et al. (2019) measure both physiology (e.g., respiration, protein content, and lipids) and gene expression on every individual. They apply two different frameworks to show how these two data types are related.

The first framework was similar to that taken by Dixon, Liao, Bay, and Matz (2018) and measured the significance of fitting the multivariate expression differences (measured as scores on a function discriminating between populations or between treatments) with the multivariate physiological data (summarized in Figure 2). A significant fit indicates that the multivariate physiological traits described by the physiological PCs are associated with the multivariate gene expression changes described by the discriminant function.

The second framework was more direct, and measured the correlation between gene expression modules and specific physiological variables. Gene expression modules were identified using a weighted gene coexpression network analysis, and their overall expression for each individual was quantified by the eigengene (the first principal component of the expression matrix). For each module, a significant correlation between this eigengene and a physiological trait supports the idea that the gene expression changes are linked to physiological changes.

Using these frameworks, they found that differences in some lipids (triacylglycerols and wax esters) correlated with the discriminant vector that described differences in gene expression between the populations. These types of lipids were significantly lower in the LU population across treatments, suggesting that the LU population had lower energy reserves. In the acidic treatment, the LU population upregulated genes with lipid-binding properties, suggesting that these individuals were mobilizing these energy reserves. Through time in the acidic treatment, however, respiration and fatty acids declined, suggesting that energy reserves were becoming depleted. In contrast, the HU population was able to maintain all physiological traits in the more acidic treatment. The HU population also upregulated ion-binding transport genes, which may be important in maintaining the carbonate chemistry of the calcifying fluid near the skeleton in acidic external conditions. At the site of calcification for many calcifying organisms, the chemistry of the internal fluid is different from the external seawater because they have specialized ion pumps, transmembrane proteins, cells, and enzymes to regulate the fluid at the site of biomineralization (Figure 1b).

In this study, the relationship between the multivariate physiological response and multivariate gene expression response (or DNA methylation response, as in Dixon et al., 2018) was determined by mapping a discriminant function estimated on one set of multivariate data onto the principal components from another set of multivariate data (as shown in Figure 2). Since principal components must be constrained to be orthogonal to each other, sometimes summarizing the data in this way can give results contrary to biological intuition (Houle, Mezey, & Galpern, 2002). Given the potential for population-by-trait or population-by-gene-expression interactions to complicate the interpretation of ordinations, the interpretation of results from this approach should be further understood through the process of analysis validation (sensu: Lotterhos, Moore, & Stapleton, 2018) before widespread use. An important next step would be to better understand how the method works in the presence of interactions, and when individuals attain the same phenotype via different gene expression pathways.

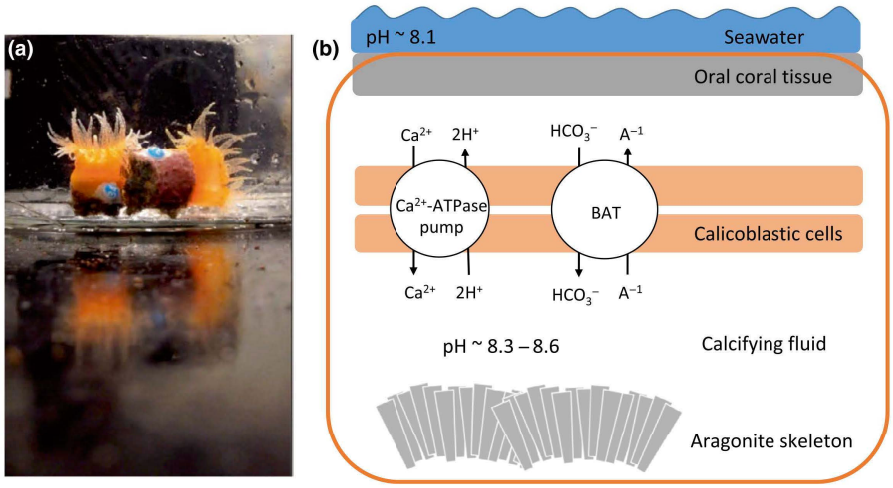
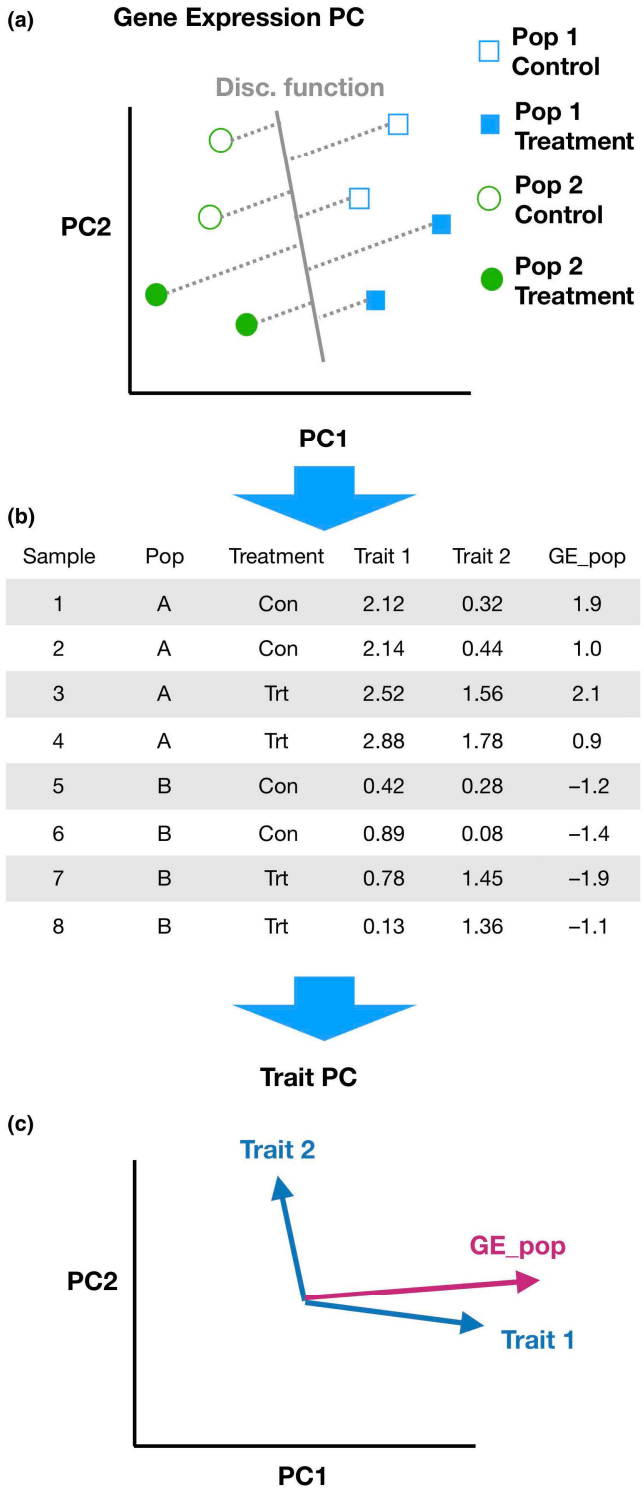


FIGURE 1 (a) Tagged *Balanophyllia elegans* corals from the experiment. Image courtesy of J. Griffiths and M. Kelley. (b) Coral calcification involves the energy intensive movement of cations and anions across cell membranes, which allows calcification of the argonite skeleton to occur. Elevation of the calcifying fluid pH occurs via removal of protons by Ca^{2+}-ATPase exchangers. Types of dissolved inorganic carbon are also transported via bicarbonate (HCO_3^-) ion transporters (BAT) and help to regulate the chemistry of the calcifying fluid. An upregulation of ion transport genes and calcium ion binding genes may help HU corals maintain energy production, pH homeostasis, and calcification. Figure courtesy of J. Griffiths and adapted from McCulloch, D'Olivo, Falter, Holcomb, and Trotter (2017)



Sample	Pop	Treatment	Trait 1	Trait 2	GE_pop
1	A	Con	2.12	0.32	1.9
2	A	Con	2.14	0.44	1.0
3	A	Trt	2.52	1.56	2.1
4	A	Trt	2.88	1.78	0.9
5	B	Con	0.42	0.28	−1.2
6	B	Con	0.89	0.08	−1.4
7	B	Trt	0.78	1.45	−1.9
8	B	Trt	0.13	1.36	−1.1

FIGURE 2 Mapping gene expression differences onto trait space. (a) First, a discriminant analysis of principal components is used on the gene expression data to find the axis in multivariate (expression) PC space along which the difference between populations is maximized. Each individual gets a score based its position in discriminant expression space (dotted lines). (b) These scores are appended to other data for each individual. "GE_pop" represents the scores from the function that discriminates gene expression between populations. (c) Principal components (PC) on the trait data is conducted to represent samples in multivariate (physiological) PC space. The GE_pop scores are used to fit the discriminant expression vector onto the ordination of the physiological PCs – much in the same way the physiological variables are visualized in physiological PC space – and the significance of this fit is assessed via a squared correlation coefficient. These last three steps are then repeated, but with a discriminant function describing differences between the treatments

Because Griffiths et al. (2019) collect corals directly from the field and acclimated them for 2 weeks prior to the experiment, they were unable to conclude that the population-specific responses to ocean acidification represent standing genetic variation that evolved via local adaptation. The results from Griffiths et al. (2019) nevertheless support the hypothesis that there are population-specific responses to ocean acidification stress. This is a notable result for ocean global change biology, because early research on ocean acidification emphasized the slow, gradual decline in pH happening in the open ocean as it reached equilibrium with CO_2 in the atmosphere. It was not recognized until recently that the pH seascape of the coastal ocean is a mosaic in space and time, with some locations experiencing extreme pH conditions on a regular basis (Chan et al., 2017). More studies like Griffiths et al. (2019) will be needed in order to paint a fuller picture of the capacity different species have to respond to this rapid and widespread global change.

AUTHOR CONTRIBUTIONS

KEL wrote the manuscript.

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