### Are there universal strategies to respond to change?

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#### Introduction

Change is a central phenomenon in all natural systems, and occurs across many scales. Conditions that are static in all aspects over time do not exist, yet life arose quickly after the formation of the planet and has persisted since. This persistence indicates that life has mechanisms that prevent complete extinction despite drastic and significant change in conditions on Earth at several points in evolutionary history. Change may resonate throughout a system and affect multiple levels of biological organization; therefore, investigating biological responses to change can be a lens for focusing integration, complexity, and predictive relationships across all scales of life. Many strategies to maintain a biological system during and after change have been studied in a variety of species and at a variety of levels, but identifying if there are universal strategies in response to change remains elusive. In this paper, we provide a framework for thinking about change across time and space, discuss the current challenges, and propose approaches for identifying universal strategies to respond to change.

Here, we consider "change" to be any shift in a biotic or abiotic factor, temporary or permanent, that has the potential to affect the functioning of life at any level. Change can be highly predictable and periodic, such as tides and seasons, or highly unpredictable, such as meteor strikes. Events that change a system can also occur over very short time scales, like a lightning strike, or over very long time scales, through earth processes like continental drift. The magnitude of perturbation can be considered a third dimension of change; a change may be a slight deviation from conditions, such as mild heat stress, or a significant one, such as a fire.

Responses to perturbations can also occur at all levels of organization (Table 1). Biological molecules respond to changes in energy inputs, cellular processes are regulated in response to environmental change, tissues may respond to changes in other systems in a multicellular organism, individuals may respond through behavior, growth, or development, and evolutionary change and community composition changes occur at the organismal level.

Processes, organisms, and ecosystems may be damaged or even extirpated by change. We may consider the threshold of tolerance to a change as the point at which life processes cease, although loss of life processes at a lower level may not translate to death of the organism or loss of the ecosystem. Alternatively, change may have positive impact on growth, survival, and ecosystem functioning, and could have positive effects on some levels and entities while having negative impacts on others. As the intensity of change increases, we may also expect non-linear responses.

Table 1. Examples of potential responses to change across levels of biological organization

Scale of effect	Brief, mild, stochastic change - an unusually warm afternoon	Predictable moderate periodic change – onset of winter	Moderate stochastic change – small brush fire	Significant stochastic change - meteor strike
molecular	Changes in the rate of enzymatic processes	Changes in gene expression in response to decreasing temperatures or daylength	Upregulation of heat shock protein, degradation of molecules in some cells	meltdown
cellular	Changes in the phospholipid composition of the cell membrane	Increase in antifreeze compounds	Some cellular death of damaged cells	meltdown
physiological	Increase in blood flow to skin surface	Slowing of metabolic rate	Response to burns, skin damage	meltdown
organismal	Movement into shade	hibernation	Altered immune response, hiding behavior, potentially death	death
Population and community	Little or no response	Evolutionary change in populations, decreased species interactions in food webs	Selection for survival mechanisms, Reduced habitat and food availability	Eventual dispersal into and adaptation to impact site
Ecosystem	Little or no response	Reductions in nutrient inputs	Altered species composition and temporary decrease in ecosystem productivity	Elimination and then redevelopment of ecosystem processes

The stochasticity vs predictability of change shapes system response. Highly predictable and cyclic change, such as circadian rhythms and seasonality, can generate processes and behaviors that anticipate the change; photosynthetic systems ramp up before sunrise, scores of genes have circadian rhythms in gene expression, and animals begin hibernating before the coldest part of the winter. Change that is more stochastic but still relatively frequent may select for responses that are triggered after the change; after initial herbivory, plants upregulate production of defensive compounds. Change that is so severe that it kills an organism results in a response at population to ecosystem levels, and potential consequent adaptation.

Perturbations may resonate throughout a system and affect multiple levels, and therefore to fully understand responses we must study them across time and space in all levels of life. Further, to determine whether there are one or multiple ways to respond to change, it is essential to know if responses to change are repeatable across systems. Our understanding of responses to a few key environmental factors, such as temperature, is extensive across many taxa and levels of organization, while the impact of other forms of perturbation, such as changes in atmospheric carbon dioxide and increased intensity of seasonality, are limited. Investigating change across all levels and systems will enable us to better understand how and why homeostasis is maintained in organisms and how selection operates to promote mechanisms that increase tolerance to change. Attempting to identify universal strategies by which organisms respond to change will also help us address diverse aspects of human health and environment, including the consequences of anthropogenic change in natural systems, disease, and changing and expanding agricultural ecosystems.

# **Key challenges**

Given the complex nature of determining if there are universal strategies for how systems respond to change, there are a number of barriers that need to be overcome to address this issue. We have identified a few important challenges, as well as potential solutions or strategies to overcome these challenges.

1. Defining change and interpreting responses across organisms/scales

Comparative approaches are critical for examining repeatability of responses. For comparative approaches to be effectively employed, a key challenge is the lack of tools and theoretical framework for defining what a similar response is across systems being compared. Similarly, how responses to change are quantified, as well as how to determine if responses from different systems are the same or different, must be established before meaningful comparisons can be made. Further, it is critical that these changes and responses are characterized in a way that is repeatable between laboratories and between organisms.

2. Generating data from diverse systems

To begin to understand if a strategy represents a general principle, it is critical to know if this strategy is employed across species and across scales. Key to identifying if a strategy is universal is taking a comparative approach. However, many responses to changes have been characterized in only a handful of species, or at only one level (ie, ecosystem, not organismal). Thus, once common metrics have been identified, obtaining more data from diverse species and systems is an additional challenge to further analyzing the universality of approaches.

3. Complexity of cross scale, cross taxa comparisons

While a significant body of scientific work relevant to this question is available in the literature, synthesizing it in a meaningful way across scales is necessary. In addition, when comparable data from large numbers of systems is obtained in the future, this data must also be incorporated in the synthesis. As the question of universality will necessitate the collection of data from large numbers of systems, analyzing this data will likely be complex, and will require expertise from across disciplines (biochemists through ecologists).

4. Removing bias barriers to characterizing change

To reproducibly identify and recapitulate any change across systems, it will be critical to accurately characterize all factors that have biologically meaningful impacts on systems.. Studies characterizing environmental parameters often fail to account for parameters not easily perceptible or quantifiable by humans. However, these biases must be removed to accurately assess all aspects of complex changes.

# Potential opportunities and solutions

Several opportunities exist for beginning to address the challenges outlined above. These include:

1. Developing tools and metrics that can be applied across organisms and scales

A key challenge we identified was comparing responses across taxa and at different complexity levels; currently, studies use a wide variety of methods for imposing and assessing change and measure a boggling array of consequences (for example, see Table 1). Initial efforts could address basic responses such as the limits at which functions or survival cease, and metrics such as activity could, in principle, be measured both at molecular (ie, enzyme) and ecosystem (ie, interactions between individuals, energy flux) across levels of complexity. Further, we recommend examining responses in creative ways. For example, while patterns may not emerge across taxa for one aspect of a response (ie, temperature at which an organism begins to have a behavioral avoidance response), they could emerge at another, such as the shape of response curves across temperatures.

2. Developing strategic comparative approaches across species and across scales

One immediate solution to the above challenges is to increase the amount of data for analysis so that comparative approaches can be employed. This will involve analyzing responses to changes across levels and taxa using standardized methods. Species examined should encompass a wide range of taxa across phylogenies and across habitats. Thus, organisms in extreme environments should also be examined, as these "extreme" cases may present important points for testing universality. Ideally, measurement of outputs at the molecular, organismal, population and ecosystem levels will help determine if there are general principles that underlie the strategies used across taxa.

3. Developing opportunities for synthesis of comparative data

In addition to generating more data, we recommend generating data in an informed way. Identifying universal strategies will require sampling across taxa and complexity levels. As a first attempt at this, generating a key list of specific systems to target for analysis that represent diverse taxa and span complexity levels to address responses to particular changes is essential. One way to generate such lists is by assembling diverse teams of researchers, from molecular and cellular biologists to ecologists to big data analysts, would serve this purpose. In addition, these types of analyses will require teams of researchers. Prioritizing assembling diverse, inclusive teams that span not just expertise, but also experimental models, geographical locations, and research and PUI institutes will be key to this process.

# **Conclusions**

Understanding the rules of life is a complex challenge and will require complex and extensive data and synthesis as well as novel, creative approaches. Because no one scientist has the extent of knowledge or time required to apply experimental or observational approaches across levels and generate a universal synthesis, we expect that a collaborative approach that is not led by a single scientist but rather coordinated by a team will be the most effective in advancing discovery. By tackling a pervasive and well-studied phenomenon such as response to change, we may begin to develop a framework for thinking about reintegration of biology across scales. A productive initial starting point may be to gather and standardize what we know about impacts of a single, well studied environmental factor, such as how temperature limits survival or function at as many levels as possible, across as many taxa as possible. This review could lead to identification of gaps in our knowledge and taxonomic representation, and start a conversation about the characteristics of common measures and testable hypotheses about universal strategies. Ultimately we hope to identify the fundamental properties that govern biological systems and the limits to life.