Essay

Beyond the Cell: Using Multiscalar Topics to Bring Interdisciplinarity into Undergraduate Cellular Biology Courses

Carolyn F. Weber**

Department of Biological Sciences, Idaho State University, Pocatello, ID 83209

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> Western science has grown increasingly reductionistic and, in parallel, the undergraduate life sciences curriculum has become disciplinarily fragmented. While reductionistic approaches have led to landmark discoveries, many of the most exciting scientific advances in the late 20th century have occurred at disciplinary interfaces; work at these interfaces is necessary to manage the world's looming problems, particularly those that are rooted in cellular-level processes but have ecosystemand even global-scale ramifications (e.g., nonsustainable agriculture, emerging infectious diseases). Managing such problems requires comprehending whole scenarios and their emergent properties as sums of their multiple facets and complex interrelationships, which usually integrate several disciplines across multiple scales (e.g., time, organization, space). This essay discusses bringing interdisciplinarity into undergraduate cellular biology courses through the use of multiscalar topics. Discussing how cellular-level processes impact large-scale phenomena makes them relevant to everyday life and unites diverse disciplines (e.g., sociology, cell biology, physics) as facets of a single system or problem, emphasizing their connections to core concepts in biology. I provide specific examples of multiscalar topics and discuss preliminary evidence that using such topics may increase students' understanding of the cell's position within an ecosystem and how cellular biology interfaces with other disciplines.

INTRODUCTION

Western science has grown increasingly reductionistic and, in parallel, the undergraduate life sciences curriculum has become disciplinarily fragmented (Odum, 1984; Lindberg, 1992; Taylor, 2010; Helfand, 2013). In the 1940s, most universities had a single biology department (Odum, 1984),

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¹Present address: Des Moines University and Osteopathic Medical Center, Des Moines, IA 50312

*Address correspondence to: Carolyn F. Weber (Carolyn.F.Weber@ dmu.edu).

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"ASCB®" and "The American Society for Cell Biology®" are registered trademarks of The American Society for Cell Biology. but many were subsequently partitioned into several departments, each one focused on a related or subdiscipline of biology (e.g., molecular biology, microbiology, ecology, evolutionary biology). Curricular fragmentation occurred alongside this partitioning and partly coincided with the rise of molecular biology in the 1950s (Mazzochi, 2011). Molecular biology fostered reductionistic science, as some accepted the notion that the complexity of life could be understood through the study of individual molecules and specific genes (Mazzochi, 2011). Indeed, narrowly focused endeavors resulted in landmark discoveries, which include the determination of DNA's structure (Watson and Crick, 1953) and its role in genetic inheritance (Avery et al., 1944). However, the shortfalls of reductionism are increasingly apparent (Gallagher and Appenzeller, 1999; Van Regenmortel, 2004) as we recognize that managing 21st-century problems (e.g., nonsustainable agriculture, infectious diseases) requires comprehending their complexity and working at disciplinary interfaces that encompass subcellular to global scales. The need for this type of work is deeply ingrained in the scientific literature from the past two decades. This

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literature is replete with interdisciplinary strategies to solve contemporary problems in the areas of conservation, sustainable agriculture, and drug development and is riddled with article titles that include phrases such as "from cells to ecosystems" and "from genes to ecosystems" (e.g., Paul et al., 2000; Torsvik and Overeas 2002; Whitham et al., 2006; Keurentjes et al., 2011; Wymore et al., 2011; Traylor-Knowles and Palumbi, 2014). In spite of the recognized need for interdisciplinary scientists and scientifically literate citizens, specialized academic departments and narrowly focused life sciences curricula prevail. This severely diminishes opportunity for undergraduates to develop cross-disciplinary thinking and problem-solving skills they will need in their professional and personal lives (Daily and Ehrlich, 1999; Brewer and Maki, 2005). In recognizing the need for undergraduates to increasingly think across scales and disciplines, the National Research Council (NRC) and the American Association for the Advancement of Science (AAAS) have both called for revisions to the undergraduate life sciences curriculum that promote integration of concepts across disciplines and different organizational levels (NRC, 2009; AAAS, 2011).

Cellular processes have ramifications at multiple scales (e.g., organismal, ecosystem, global), but they are not routinely taught in the context of this hierarchy. Instead, a typical undergraduate biology curriculum has individual courses dedicated to single levels within this hierarchy (e.g., ecosystem science, ornithology, cellular biology). When this hierarchy is not presented in a single classroom, the emergent properties at larger scales (e.g., ecosystem) are not conveyed; such properties cannot be directly predicted from studying lower levels of organization in isolation, as the behavior of a molecule or gene is usually altered when placed within the overall metabolic and genetic contexts of an organism and the environmental conditions the organism experiences (Van Regenmortel, 2004; Mazzochi, 2011). For instance, an infectious disease may be discussed exclusively in terms of the cellular-level mechanisms by which the pathogen evades immune system detection in the human body. However, a more complete understanding of the nature of an infectious disease requires consideration of the natural reservoirs that harbor the pathogen, contribute to the means by which it is spread, and influence the evolution of its pathogenicity. This is exemplified by recently emerging infectious diseases, 75% of which are zoonotic and carried by wildlife (Beck et al., 2012). This is not to say that studying single molecules and genes is not fruitful, but truly understanding organismal phenotypes and their relationships with ecosystem characteristics requires studying molecular and genetic processes within the complex biological systems of which they are a part (Van Regenmortel, 2004; Mazzochi, 2011). In this sense, reductionism and holism are not opposed to each other but are complementary and necessary in the study of complex biological problems (Fang and Casadevall, 2011).

Typical cellular biology curricula and textbooks (e.g., Alberts *et al.*, 2014) overwhelmingly focus on activities within individual cells (e.g., metabolism, growth, DNA replication), rarely making connections to scales beyond an organism. This hinders student acquisition of skills associated with systems thinking, which enable one to process multiple facets of a given situation and how they are interrelated (Cabrera and Cabrera, 2015). These skills are particularly important in solving real-world problems in, for example, sustainable development (e.g., grazing, forestry; Vitousek et al., 1997), which requires that people maintain human values of well-being and balance them with concern for ecosystem health (Forget and Lebel, 2001; Walker and Salt, 2006; Nelson et al., 2010). Few of society's most significant problems fall within the confines of a single discipline (Daily and Ehrlich, 1999), and systems-thinking skills facilitate integrating multiple disciplines in problem-solving efforts. An example of a real-world problem that is best managed by using systems-thinking skills is crop destruction by invasive insect species. Genetic engineers, working exclusively at the subcellular level, may be able to engineer the crop to produce a pesticide against the target insect. However, examining the toxicity of this pesticide on nontarget organisms and considering its impact on overall ecosystem health are necessary to ensure that solving the problem within the confines of molecular genetics does not prove more detrimental than the original problem (Wolfenbarger and Phifer, 2000).

All undergraduates, not just those who go on to be professional biologists, can benefit from understanding the ramifications of cellular-level processes at multiple scales. Irrespective of profession, college graduates are increasingly confronted with managing real-world problems as members of cross-disciplinary teams (NRC, 2003; Brewer and Maki, 2005; Pennington, 2008) and with making important decisions in their own lives about issues rooted in biology (Robinson and Crowther, 2001; Hoskinson et al., 2013). Personal health and lifestyle are prime examples of the latter. Completion of the human genome sequence has lead to increased effort to understand the regulatory biochemical pathways it encodes and how environmental parameters may alter gene expression in ways that trigger various disease states. We are moving into an era when understanding risk factors for human health is possible. This allows us to increasingly embrace preventative medicine, redefining health as something more than the mere absence of disease (Forget and Lebel, 2001). However, to optimize health, society must better understand how the human body and its surrounding ecosystem are simultaneously affected by multiple environmental factors (e.g., climate, pollution, biotic interactions) through time. For example, if one has a set of genes whose expression has been correlated with the onset of breast cancer, it is useful to know what environmental factors influence these genes' expression and how one's lifestyle could be altered to mitigate risk. For society to derive maximal benefit from scientific findings, institutions of higher education must turn out systems thinkers and, therefore, redesign curricula to serve this purpose.

The above examples establish the value of skills associated with systems thinking, but the nature of human cognitive functioning makes these skills difficult to acquire. First, understanding the complex biology around us is easier if we focus on its individual aspects rather than trying to assimilate everything at once (Daily and Ehrlich, 1999). The brain has a natural tendency to simplify cognitive functioning by breaking down novel information into smaller pieces and categorizing them by matching them with previously developed cognitive databases built from different but related experiences (Lilienfeld *et al.*, 2015). This process, referred to as top-down processing, is how we construct knowledge databases, create meaning from our experiences, and, essentially, learn (Lilienfeld *et al.*, 2015). For example, when one views words on a page, top-down processing connects these images to previously acquired knowledge of words, making it possible to read a book one has never read before. However, developing skills associated with systems thinking is cognitively challenging, because it depends on the ability to simultaneously utilize multiple knowledge databases and compute how they are related to one another. Our tendency to simplify cognitive functioning may partly explain our propensity to fragment the undergraduate life sciences curriculum into many subdisciplines. Although courses in each subdiscipline offer the opportunity for students to develop new knowledge databases, memory recall from such databases alone will not assist people in managing the world's complex problems (Hoskinson et al., 2013); more important, the ability to determine how one aspect of the problem is related to the others. Thus, the contemporary faculty member should focus less on instilling knowledge databases in students and more on being a tour guide who helps students see connections between disciplines and recognize when they may need to consult other areas for expertise when they do not know something (AAAS, 2011). For instance, students in a cellular biology course may be introduced to the subcellular mechanisms of how antibiotics prevent growth of pathogenic organisms, but with regard to taking a knowledgeable stance on whether or not antibiotics should be incorporated into livestock feed, students should consult what is known about the ecological consequences of antibiotic contamination of the environment (e.g., increased prevalence of antibiotic-resistant bacteria).

This essay outlines the rationale for incorporating multiscalar topics into the undergraduate cellular biology curriculum. Utilizing such topics embraces the AAAS five core concepts for biological literacy (Table 1) and recommended core competencies, including the ability to "tap into the interdisciplinary nature of science," "communicate and collaborate with other disciplines," and "understand the relationship between science and society" (AAAS, 2011). This is also in line with recommendations from the NRC that biology curricula be revised to force students to "integrate concepts across levels of organization and complexity" (AAAS, 2011, p. ix). The use of multiscalar topics may also provide a mechanism to overcome cognitive barriers to facilitate skills associated with systems thinking, which include thinking across disciplines. Specific examples of cellular biology topics that can be discussed across multiple scales are provided along with some preliminary evidence that utilizing such topics in the classroom may broaden student thinking.

RATIONALE FOR EXPLORING MULTISCALAR TOPICS IN CELLULAR BIOLOGY

Cellular-Level Processes Have Ramifications at Larger Scales That Are Relevant to Everyday Life

Cellular processes influence phenomena at large scales (i.e., ecosystem), and developing an understanding of this promotes the development of skills associated with systems thinking. Multiscalar discussions may also be pedagogically advantageous for teaching and learning cellular biology. Humans do not live at the cellular level. As a result, undergraduates do not have direct life experiences with the inner workings of a cell that they can use as a foundation upon

Table 1.	The five	core	concepts	for	biologia	al literacy ^a
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Concept	Description
Evolution	The diversity of life evolved over time by processes of mutation, selection, and genetic change.
Structure and function	Basic units of structure define the function of all living things.
Information flow, exchange, and storage	The growth and behavior of organisms are activated through the expression of genetic information in context.
Pathways and transformations of energy & matter	Biological systems grow and change by processes based upon chemical transformation pathways and are governed by the laws of thermodynamics.
Systems	Living systems are interconnected and interacting.

which to build their knowledge database of cellular characteristics and processes. This can make cellular biology an abstract subject. However, when cellular structure and function are placed in the context of large-scale phenomena and problems that do affect people's daily lives, such as disease spread (Lee, 2001; de Magny and Colwell, 2009), crop productivity (Keurentjes *et al.*, 2011; Metson *et al.*, 2013), and even weather patterns (Figure 1; Christner, 2012), a context for learning the underlying cellular biology can be established.

Familiar contexts may assist in overcoming cognitive barriers to developing skills associated with systems thinking. Familiar contexts open up opportunities to teach through narratives, such as news stories that people hear everyday, which are key in how humans develop an understanding of the world around them (Ball, 1998). Accordingly, the use of narrative has been shown to improve student performance (Arya and Maul, 2012), and it also increases the chances of emotionally engaging students in the course material; this can increase the scope of attention and broaden habitual modes of thinking, thus increasing potential for learning (Frederickson and Branigan, 2005). Narratives and emotional engagement may resonate with previous life experiences and course work for which students have previously established knowledge databases. In this case, cellular-level information can be tied to these preexisting databases, facilitating learning by activating consciousness and creating meaning for the new material (Hill, 2001; Jandu, 2012). Learning in this manner also deemphasizes mastering course content strictly via rote memorization, which requires constant laborious effort (Jensen, 1996). Lowering cognitive barriers to learning cellular biology by teaching it in a familiar context also opens up the opportunity for students to discover their own misconceptions about biology in the world around them (NRC, 2000). Revising misconceptions can make the material more memorable and enhance student ability to recall it (Hill, 2001).

Multiscalar discussions also create opportunities to connect cellular biology to other disciplines within and outside the life sciences (Nelson *et al.*, 2010). Couching protein structure and function in the context of weather patterns connects cellular biology to disciplines as diverse as meteorology, physics, chemistry, ecology, and even biotechnology

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Figure 1. Questions that provide a framework for mapping a multiscalar topic, such as the bioprecipitation cycle, to the five core concepts for biological literacy (AAAS, 2011) and content specific to undergraduate cellular biology courses. Core concepts targeted by the questions are shown in parentheses. Core concepts are fully detailed in Table 1.

(Figure 1). The connection to biotechnology can be made, because ice-nucleating proteins are the active ingredient in a product called Snomax, which is used at ski resorts to increase the efficiency of snow production (Christner, 2010). Other multiscalar topics presented in Table 2 and described

in greater detail below connect cellular biology topics to diverse disciplines such as sociology, agriculture, nutrition, climate change, and politics. This interdisciplinarity satisfies undergraduate desires to see more connections across the curriculum and between various disciplines (AAAS, 2011).

Table 2	. Examples of multiscalar	topics that link cell	lular biology to th	e five core conce	pts for biological	literacy,ª everyday	life, and other
discipli	nes ^b						

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Cellular biology topic	Multiscalar topic	Core concepts covered ^c	Relevance to everyday life	Other relevant disciplines	Resources
Elemental needs of cells	Impacts of declining phosphorus resources on crop production	E, S, I, SF, P	Future of food production and the need for sustainable agriculture	Agriculture, economics, politics, nutrition, ecology, and biotechnology	Metson <i>et al.,</i> 2013
Protein structure and function	Ice-nucleating proteins in bacteria and their impact on weather patterns	E, S, I, SF, P	Weather patterns, crop damage, and artificial snow for winter sports	Physics, meteorology, agriculture, economics, ecology, and biotechnology	Figure 1; Christner, 2012
Cell growth and division	Vibrio cholera, outbreaks and natural reservoirs and how they are impacted by climate change	E, S, I, SF, P	Disease spread and climate change	Sociology, epidemiology, politics, ecology, and climate change	Lee, 2001; de Magny and Colwell, 2009
DNA structure and function	Epigenetic inheritance and its role in human behavior	E, S, I, SF, P	Human personality, behavior, and lifestyle	Psychology, sociology, and politics	Rice et al., 2012
Cell–cell communication	Role of antibiotics and hormones as signaling molecules in microbe- microbe and plant- microbe interactions	E, S, I, SF, P	Bioprospecting in nature for antibiotics to fight human disease and using plant hormones to promote plant growth	Agriculture, medicine, microbiology, plant physiology, and biotechnology	Davies, 2006; Weber, 2014
Genetic inheritance	How the evolution and genetic engineering of wheat has influenced gluten consumption	E, S, I, SF, P	Trends in gluten consumption and its impact on human health	Agriculture, medicine, nutrition, plant genetics, and genetic engineering	Bronski and Jory, 2012

^aTable 1; AAAS (2011).

^bThese topics have been utilized in cellular biology lecture and/or laboratory courses at Idaho State University (Pocatello ID) that are sophomore-level courses predominately attended by pre-health profession students and biology majors.

^cCore concepts emphasized by the various topics are bolded and are denoted as follows: E, evolution; S, systems; I, information flow, exchange, and storage; SF, structure and function; P, pathways and transformations of energy and matter.

Making these connections also helps students develop core competencies outlined by the AAAS (2011), which include the abilities to "tap into the interdisciplinary nature of science," "communicate and collaborate with other disciplines," and "understand the relationship between science and society." Mastering these core competencies will facilitate student success in the future as members of interdisciplinary teams, which are becoming commonplace (Brewer and Maki, 2005).

Illuminating multiscalar impacts of cellular processes and connections between seemingly disparate disciplines highlights society's need for systems thinkers to manage looming problems. By the year 2050, the global population is projected to reach nine billion, and agricultural yields will need to increase by 70–100% to generate adequate food supply (American Academy of Microbiology [AAM], 2012). A plant geneticist alone could address this problem by engineering faster-growing crops. However, rapidly growing plants will require increased quantities of nutrients, such as phosphorus (P) to support the rapid manufacture of P-containing macromolecules (e.g., DNA, phospholipid bilayers, adenosine triphosphate, ribosomes) and thus growth (Sterner and Elser, 2002). As P resources diminish, using more fertilizer is simply not a feasible solution; additionally, 77% of the world's remaining phosphate mines are in a single country (Morocco), and any increase in demand for these resources would likely exacerbate political and economic problems (Karp and Shield, 2008; AAM, 2012; Metson et al., 2013). Most cellular biology courses cover topics such as the elemental needs of cells, structure of macromolecules, and cellular growth, and the food production crisis can bring the societal relevance of these cellular biology topics into focus. Developing sustainable agricultural practices that fulfill human needs requires systems thinking by scientists of many disciplines and their working together with social scientists and world leaders to consider the multiple facets of this problem. Pennington (2008) notes that one of the biggest barriers to solving such problems is the lack of conceptual frameworks for integrating across biotic, human, geological, and built domains. Therefore, exposing undergraduates to connections among disciplines and real-world problems should prove valuable in facilitating their success in the future.

Deep Exploration of Multiscalar Topics Unites Diverse Disciplines by Linking Them to the Core Concepts for Biological Literacy

Exploring multiscalar topics takes time and necessitates reducing overall course content, but the benefits may be multifold. Pursuing relatively few topics in greater depth has been associated with increased student comprehension (Hardiman, 2012), improved student attitude toward science (Sundberg *et al.*, 1994), and increased opportunity for using active-learning activities that facilitate student engagement (Gregory *et al.*, 2011). The association between reduced course content and improved student comprehension and attitude may be especially critical to consider in efforts to reverse declining interest in science, technology, engineering, and mathematics careers in the United States and increase overall biological literacy (AAAS, 2011).

Pursuing multiscalar topics in depth provides the opportunity to root each one, and the multiple disciplines they encompass, in the five core concepts for biological literacy

(Table 1; AAAS, 2011). Doing this makes it possible to illustrate the core concepts in diverse ways and generate more opportunity to develop conceptual frameworks that integrate factual knowledge and concepts. Additionally, this approach enables students to observe similarities and make connections between even seemingly unrelated topics in biology (Figure 2). For instance, two topics that initially appear to have very little in common are eutrophication and cancer. In fact, these two topics would rarely, if ever, be discussed in a single course. Nonetheless, these two topics are rooted in the same biological principles (Figure 2). Both eutrophication and cancer illustrate the role of P in energy transformation and in DNA's structure and how rapid cellular growth results in rapid uptake of P and disruption of chemical homeostasis in the environment, be it an aquatic ecosystem or a human being (Sterner and Elser, 2002; Elser et al., 2003, 2007).

The core concepts (Table 1) were outlined to achieve six core competencies (AAAS, 2011) and address four major challenge areas outlined in the National Research Council's A New Biology for the 21st Century (NRC, 2009). The major challenges include generating food plants that grow sustainably in a changing environment, understanding and sustaining ecosystem function and biodiversity in the face of rapid change, expanding sustainable alternatives to fossil fuels, and understanding individual health. Although these areas may not appear to encompass all of biology, the NRC noted that, because biological systems have so many similarities, technologies developed to address these challenge areas will grow capabilities across the entire field. This is even more reason to discuss diverse topics in the context of the core concepts. Drawing connections between seemingly disparate topics may be the very key to future innovations. Additionally, applying the core concepts to multiscalar topics provides the opportunity to link these concepts to problems encountered beyond the classroom and make biological literacy relevant to everyday life. For example, understanding the basic characteristics of cellular growth could apply to understanding a bacterial ear infection and the increased prevalence of antibiotic-resistant bacteria in the environment and could provide students with the knowledge to make the decision of whether or not to take antibiotics prescribed by a physician.

EXAMPLES OF MULTISCALAR TOPICS

A major concern with any curricular revision is that the perceived fundamentals of a given discipline remain intact. Widely used textbooks for undergraduate cellular biology courses (e.g., Cooper and Hausman, 2013; Karp, 2013; Alberts et al., 2014) generally cover a selection of the following topics: cellular characteristics and chemical building blocks, protein structure and function, energy generation, biosynthesis, chromosomes, DNA replication, DNA repair and recombination, transcription, translation, gene/genome evolution and manipulation, membrane structure and transport, energy acquisition from food, intracellular compartments and transport, cell communication, the cytoskeleton, mitosis, meiosis, heredity, tissues, and cancer. In addition to multiscalar topics already presented above (i.e., bioprecipitation, food crisis), three examples of multiscalar topics that encompass textbook fundamentals and core concepts are described in the following sections (Table 2). It should be noted that the topics presented



Figure 2. The topics of eutrophication and cancer share common links (indicated by lines) to the five core concepts for biological literacy (Table 1; AAAS, 2011), which illustrate their common biological foundations, even though these two topics are rarely, if ever, discussed in the same undergraduate course. Arrows link chains of events leading up to or resulting from cancer and eutrophication.

in this article may not illustrate all core concepts equally well, and depending on the instructor's presentation of these topics, different core concepts can be emphasized more than others.

Genome Evolution: Has Polyploidy Contributed to the Rise of Gluten Intolerance?

Wheat has evolved substantially since its domestication 10,000 years ago in the Fertile Crescent of Mesopotamia (Kasarda, 2013). Human-imposed selection for desirable characteristics and genetic manipulation have tripled crop yields from the 1950s through the 1990s (Bronski and Jory, 2012). This has led to increased incorporation of wheat-based products into modern human diets; in 2008, the estimated consumption per capita was 136.6 pounds of wheat (Bronski and Jory, 2012). Wheat contains gluten, a storage protein that is used to fuel the growth of a sprouting seed, and also makes flour ideal for creating desirably textured bread (Bronski and Jory, 2012). However, gluten is composed of proline-rich proteins (glutenin and gliadin) that remain virtually undigested in the stomach. Increased gluten content, along with other factors (e.g., wheat type and genetics, agronomic practices; Kasarda, 2013) may link increased consumption of wheatbased products with gluten intolerance and celiac disease

(complete gluten intolerance), which was 4.5 times more prevalent in 2009 than in the 1950s (Bronski and Jory, 2012).

Modern wheat (*Triticum aestivum*) has 42 chromosomes (hexaploid) acquired through polyploidy, while its ancestors, einkorn (14 chromosomes, diploid) and emmer (28 chromosomes, tetraploid), have smaller genomes (Bronski and Jory, 2012). Emmer's chromosomes came from two different wheat genomes, denoted A and B in wheat genetics, but modern wheat also contains chromosomes from wheat genome D, which comes from a wild grass species (*Triticum tauschii*; Salentijn *et al.*, 2009; Kasarda, 2013). The gluten genes encoded by genome D are preferentially expressed, and the resulting gluten is more toxic than that produced by genomes A and B (Salentijn *et al.*, 2009), which may be key in the rise of gluten intolerance (Bronski and Jory, 2012).

Cell Growth and Division: Vibrio cholerae and Climate Change

Cholera, a life-threatening illness caused by the bacterium *Vibrio cholerae*, is characterized by severe diarrhea and dehydration (Lee, 2001). *V. cholerae* produces the cholera toxin, which leads to the ADP-ribosylation of a G protein and eventually elevated levels of cyclical AMP that create electrolyte imbalance in cells (Bharati and Ganguly, 2011).

Throughout history, outbreaks of cholera have been common in South Asia, but the pathogen eventually spread to Europe, Africa, and the Americas (Lee, 2001). Poor drinking water sanitation contributed to many outbreaks in these regions (Lee, 2001), but outbreaks in Bangladesh were found to occur with a degree of periodicity, coinciding with El Niño events and changing ocean current patterns (de Magny and Colwell, 2009). *V. cholerae* lives in several natural reservoirs but most notably in association with marine phytoplankton (Tamplin *et al.*, 1990), in which it would feed on the phytoplanktons' metabolic waste products (Murray *et al.*, 1986). When phytoplankton abundance increases in response to warmer surface water temperatures during El Niño, *V. cholerae* also proliferates, increasing human contact with the pathogen (de Magny and Colwell, 2009).

Cell–Cell Signaling: Antibiotics and Hormones in Organismal Communication

Hormones and antibiotics are commonly thought of in the context of human health, but these molecules have been utilized by microorganisms and plants as signaling molecules throughout the course of evolution, possibly even having played roles in the evolution of muticellularity (Davies, 2006; Verhage et al., 2010). With the need to ramp up food production to feed the world's burgeoning population, scientists are interested in looking to nature for solutions and perhaps in capitalizing on plant growth-promoting hormones that are produced by microbes (e.g., Contreras-Cornejo et al., 2009). Likewise, as the antibiotic resistance crisis intensifies (World Health Organization, 2001), there is renewed interest in bioprospecting for novel secondary metabolites that might have yet to be discovered antibiotic properties (e.g., Weber and Werth, 2015). Bioprospecting efforts are targeting the members of the Streptomyces genus and related genera, which already produce more than 50% of the world's clinically useful antibiotics (Liu et al., 2013) but still harbor a plethora of uncharacterized secondary metabolite-producing pathways in their genomes that may produce novel antibiotic compounds (Bentley et al., 2002).

DISCUSSION

The scientific and pedagogical literature from the past 30 years brims with outcries for interdisciplinarity in response to society's problems becoming increasingly complex (e.g., Odum, 1984; Brewer and Maki, 2005; Whitham et al., 2006; AAAS, 2011; Wymore et al., 2011). Accordingly, many universities have made interdisciplinarity a goal (Sá, 2008), but the extent to which this goal has been achieved remains uncertain (Rhoten and Pfirman, 2006), and reductionistic pedagogy persists (Elkana et al., 2010), likely due to administrative and cognitive factors, among others. However, multiscalar topics can introduce interdisciplinarity into cellular biology, a core course in the life sciences curriculum, without need for massive educational reform at the institutional level. Revising course content to include such topics does present some of its own challenges, but they can be overcome using strategies discussed in the following paragraphs, and they are overshadowed by the benefit of potentially broadening student thinking.

One of the biggest challenges in incorporating multiscalar topics into any course is the tendency for university faculty members to think within the confines of their expertise. Narrow areas of faculty expertise combined with the absence of multiscalar topics from cellular biology textbooks and other educational resources resist inclusion of such topics in the curriculum. One strategy to circumvent this problem is to develop courses taught by teams of faculty who have members from different areas of expertise. This approach, however, is often met with administrative resistance (Brewer and Maki, 2005). At many institutions, faculty progress is quantified by metrics that emphasize research achievement (e.g., number of publications, research funding). Team teaching and course revision require a substantial amount of time for planning and coordination, which is typically viewed as a distraction from research. Additionally, quantifying faculty teaching loads in the case of team-taught courses is fraught with problems of splitting course credits, resulting in measures that do not adequately capture course-development efforts (Brewer and Maki, 2005). In addition to institutional emphasis on research achievements, life sciences faculty members "grow up" in graduate training programs in which research success is highly coveted (Golde and Gallagher, 1999; Helfand, 2013) and develop "research identities" but not "teaching identities" (Brownell and Tanner, 2012). The latter seems to be a significantly less-valued aspect of a faculty member's professional identity (Brownell and Tanner, 2012), reinforced by lack of institutional reward for innovative teaching. This creates reluctance among faculty to participate in pedagogical change (Brownell and Tanner, 2012), even though research communities depend on science education to renew and replenish them (Miller, 2010).

Still, although effortful, taking on the task of revitalizing a course to better serve students in an ever-changing world can be intellectually stimulating for professors and students alike, especially when some of the workload of course development is placed on the students. Student-centered approaches could be utilized in a lecture course by having students generate topics and questions they are interested in learning more about. Several studies indicate that courses centered around student questions and inquiry may enhance learning and attitude (e.g., Shodell, 1995; Howard and Miskowski, 2005). Additionally, as the faculty member goes outside his or her expertise and engages students in the process, he or she sets an excellent example for students of what it takes to be a lifelong learner. Students model their instructors, and if faculty model social responsibility and the importance of biological literacy, they can inspire both majors and nonmajors to do the same (Chamany et al., 2008).

One way to relieve some of the course instructor workload is to simply charge students with connecting large-scale phenomena they are interested in with the underlying cellular biology and the core concepts. I used this approach by creating a blog called *Cells and Beyond* (https://cellsandbeyond .wordpress.com); students were required to choose topics relevant to everyday life (e.g., oil spills, Ebola outbreaks, clean energy) and explain the underlying cellular biology. This type of assignment also capitalizes on the technological era, forcing students to assimilate facts that are at their fingertips (AAAS, 2011). Eliciting student ideas also establishes a baseline of student conceptions for both student and instructor and provides a starting point for revising any preexisting

Book	Related cellular biology topics	Links to other disciplines
Pollan M (2006). The Omnivore's Dilemma: A Natural History of Four Meals, New York: Penguin, 450 pp.	Photosynthesis, chemical building blocks of cells, and growth and metabolism	Agriculture, economics, politics, food science, nutrition and dietetics, and ecology
Rohwer F (2010). Coral Reefs in the Microbial Seas: The Influence of Fishing, Nutrients, Bacteria, Viruses, and Climate Change on Nature's Most Wondrous Constructs, Basalt, CO: Plaid Press, 201 pp.	Photosynthesis, chemical building blocks of cells, and growth and metabolism	Aquaculture, meteorology, chemistry, conservation, sociology, ecology, economics, and tourism
Ohlson K (2014). The Soil Will Save Us, New York: Rodale, 256 pp.	Photosynthesis, chemical building blocks of cells, and growth and metabolism	Agriculture, economics, politics, conservation, and ecology
Hempel S (2007). The Strange Case of the Broad Street Pump, John Snow and the Mystery of Cholera, Berkeley: University of California Press, 321 pp.	Growth and cellular signaling cascades	Epidemiology, microbiology, and immunology
Cordain L (2011). The Paleo Diet: Lose Weight and Get Healthy by Eating the Foods You Were Designed to Eat, Hoboken, NJ: Wiley, 266 pp.	Cellular metabolism and energy generation and genetic inheritance	Physiology, agriculture, sociology, food science, nutrition and dietetics, psychology, and evolution
Bronski P, Jory MM (2012). The Gluten-Free Edge: A Nutritional and Training Guide for Peak Athletic Performance and an Active Gluten-Free Life, New York: The Experiment, 374 pp.	Genetic inheritance, genome evo- lution, and gene expression	Agriculture, physiology, food science, and nutrition and dietetics
Coyle D (2009). The Talent Code, New York: Random House, 256 pp.	Cellular structure and function, cellular differentiation, and growth	Neuroscience, psychology, and sociology

Table 3. Examples of books in the popular science literature that can be used to provide a familiar context for students to use as a foundation for learning the underlying cellular biology

misconceptions (Hewson *et al.*, 1998), broadening thought patterns and thus honing skills associated with systems thinking. A similar but more directed approach might be to provide students with specific topics from popular news sources (e.g., *Scientific American*, National Public Radio) and require them to dig into the underlying cellular biology. For instance, a news article about an oil spill can quickly engage students in material about bioremediation and cellular metabolism. Popular books can also provide great ideas for topics (see Table 3). *The Talent Code*, by Daniel Coyle (2009), provides an interesting account of how people can unlock their talents; this topic is rooted in the myelination of axons, which provides a framework for discussing cellular structure and function as well as differentiation and growth.

Integrating multiscalar topics into cellular biology is an approach that is aligned with recommendations for revising undergraduate life sciences education outlined by the NRC (2009) and the AAAS (2011). Both of these organizations have embraced interdisciplinarity through their calls for biology curricula to meld principles across organizational levels of varied complexity and to strive toward improving student communication across disciplinary boundaries and understanding of how science interfaces with society (NRC, 2009; AAAS, 2011). The recommendations of these two agencies are founded on the misalignment of the needs of science and society with what some current pedagogical practices accomplish. As a result, it is fair to hypothesize that approaches aligned with the above recommendations, such as the multiscalar approach outlined within, represent improvements on facets of life sciences curricula that are devoid of real-world applications. However, to ensure that life sciences education moves forward using evidence-based teaching methods (e.g., Labov et al., 2009) proper assessment of the multiscalar approach outlined within is warranted. The metrics that would be appropriate in assessing the effectiveness of the approach are multifaceted and depend on the specific learning goals or objectives of the course in which the approach is being used. Metrics that might be best suited for quantifying the overall effectiveness of using multiscalar topics in a course like cellular biology would measure cognitive gains associated with scientific literacy. Scientific literacy is beneficial to the diverse population of students that may attend such a course, even though they may represent diverse academic majors and professional goals. To this end, assessments designed to quantify student learning gains with respect to the core concepts (AAAS, 2011) may serve as a metric of the method's effectiveness to increase scientific literacy in a diverse population of students.

Using such an assessment, I have evidence that utilizing multiscalar topics that are relevant to everyday life can broaden student definitions of what systems are and revise student misconceptions about biology (Weber, 2014). In a cellular biology laboratory course (Idaho State University, Pocatello, ID), I implemented a module that was centered around the involvement of hormones and antibiotics in cell-cell signaling in the environment. Students read peerreviewed literature describing the role of antibiotics and phytohormones in nature (Davies, 2006; Contreras-Cornejo et al., 2009). Based on pre- and postmodule surveys asking the students to connect the topics of hormones and antibiotics to the core concepts (AAAS, 2011), student learning gains were demonstrated (Weber, 2014). Premodule surveys indicated that students overwhelmingly understood hormones and antibiotics in the context of human development and health. In this module, hands-on experiments demonstrating the ability of microbes to promote the growth of plants and

to communicate with each other helped students develop a firmer grasp on how these molecules are utilized out in nature and how they might be applied in agriculture to mitigate the food shortage problems (AAM, 2012). Postmodule surveys indicated that learning gains were made with respect to the "Systems Concept" (Table 1) in the context of both antibiotics and hormones as students could effectively describe hormones and antibiotics as signaling molecules utilized by plants and microbes as well as within the human body (Weber, 2014). The "systems concept" was the only core concept for which learning gains were observed with respect to both topics presented in the laboratory module, but substantial learning gains were especially evident for the "pathways concept" with respect to antibiotics. Although some multiscalar topics may showcase some core concepts better than others (Table 2), evidence that multiscalar topics can elicit learning gains with respect to core concepts other than the systems concept is a positive outcome. Another positive outcome of the laboratory module detailed in Weber (2014) was that some students also indicated that they had revised their misconception that antibiotics are chemicals that are solely synthesized by people working in biotechnology labs.

CONCLUSIONS

Exploring multiscalar topics in undergraduate cellular biology courses help to cultivate skills associated with systems thinking and biological literacy in students by overcoming cognitive barriers and the tendency for cellular biology to be an abstract subject. The approach described above satisfies cries from the educational sector to emphasize depth versus breadth and contemporary student desires for a more integrative curriculum. Multiscalar topics may help students better understand the position of cells within an ecosystem and introduce them to the importance of systems-thinking skills in managing the world's complex problems. Reductionistic science has provided us with powerful tools (e.g., genetic engineering), but that power can overcome us if we do not carefully consider the potentially devastating consequences at multiple scales when problems are solved within the confines of a single discipline. Discussing this with students can help them generate an awareness of this problem as they will be increasingly confronted professionally and personally with complex problems rooted in biology.

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