

Article

A Model of How Different Biology Experts Explain Molecular and Cellular Mechanisms

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Constructing explanations is an essential skill for all science learners. The goal of this project was to model the key components of expert explanation of molecular and cellular mechanisms. As such, we asked: What is an appropriate model of the components of explanation used by biology experts to explain molecular and cellular mechanisms? Do explanations made by experts from different biology subdisciplines at a university support the validity of this model? Guided by the modeling framework of R. S. Justi and J. K. Gilbert, the validity of an initial model was tested by asking seven biologists to explain a molecular mechanism of their choice. Data were collected from interviews, artifacts, and drawings, and then subjected to thematic analysis. We found that biologists explained the specific activities and organization of entities of the mechanism. In addition, they contextualized explanations according to their biological and social significance; integrated explanations with methods, instruments, and measurements; and used analogies and narrated stories. The derived methods, analogies, context, and how themes informed the development of our final MACH model of mechanistic explanations. Future research will test the potential of the MACH model as a guiding framework for instruction to enhance the quality of student explanations.

INTRODUCTION

Explaining a biological phenomenon effectively is a cornerstone of success in biology, and curriculum policy documents echo the importance of this ability (American Association for the Advancement of Science [AAAS], 2011). When explaining natural phenomena, biologists describe mechanisms that regulate the behaviors of complex molecular and cellular systems, but explaining these mechanisms in the classroom presents a challenge, due to their complicated, intangible, and abstract nature. There is a need to make the

molecular and cellular mechanisms explained by biologists more comprehensible to students. To understand how biologists explain, we address here the following research questions: What is an appropriate model of the components of explanation used by biology experts to explain molecular and cellular mechanisms? Do explanations made by experts from different biology subdisciplines at a midwestern U.S. research university support the validity of this model? A valid conceptual model of components biologists include when they explain molecular and cellular mechanisms may help biology educators to both better understand the practices of science and better address the challenges faced by students.

This report overviews the issues surrounding biological explanations and focuses on molecular and cellular mechanisms as a key type of biological explanation. For the purpose of the present study, a biological mechanism explains how the component entities of a biological phenomenon interact at the molecular, microscopic, and macroscopic levels to produce detectable changes in state, activities, and spatial and temporal organization. This definition was adapted from van Mil *et al.* (2013), who applied work in the philosophy of science to characterize the chemotactic behavior of an *Escherichia coli* bacterium as an example. This definition

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provides a useful starting point for considering the content of explanations used in biology to teach molecular mechanisms, but research is needed to learn whether scientists across multiple biology subdisciplines actually reason back and forth between cells and molecules (as described by van Mil *et al.*, 2013) in their models of molecular mechanisms based on bacterial chemotaxis. Through a brief review of the literature, we first survey what it means to explain molecular and cellular mechanisms by comparing what scientists, science educators, and others have identified as challenges when explaining biological mechanisms. Then, we propose and validate a model of explanations of molecular and cellular mechanisms for a variety of biological contexts with the ultimate goal of assisting educators in training biology students to explain in ways that are congruent with the practices of biology. Throughout this report, we use the term “model” as a noun to refer to the conceptual representation of abstract components communicated by biologists when explaining molecular and cellular mechanisms and as a verb to describe methods used to identify those components.

BACKGROUND AND RESEARCH QUESTIONS

Recent reports call for curriculum reform in the biological sciences to better prepare future scientists for doing research and to increase the scientific literacy of college graduates (National Research Council, 2009; AAAS, 2011). According to the *Vision and Change* report (AAAS, 2011), biological core concepts and core competencies should be taught at the undergraduate level, including the ability to apply the process of science, to use quantitative reasoning, to model and simulate, to communicate and collaborate across disciplines, to tap into interdisciplinary approaches, and to relate science with society. Among the core competencies, “a key recommendation is that biology courses and curricula must engage students in how scientific inquiry is conducted, including evaluating and interpreting scientific explanations of the natural world” (AAAS, 2011, p. xiii). However, despite this focus on scientific explanations, these documents do not define what it means to create a scientific explanation.

Some biologists distinguish biological explanations by the types of questions that are being answered. According to Mayr (2004), biologists pursue two kinds of explanations: proximate causal explanations, which address “what” and “how” questions, and ultimate causal explanations, which answer “why” questions. Studies of proximate causes of molecular and cellular biology are grounded in a mechanistic model of scientific explanations, whereas ultimate causes are rooted in grander, more complex evolutionary theories. According to van Mil *et al.* (2013), when researchers explained the mechanism for chemotaxis in *E. coli*, they asked “how” questions, subdivided activities based on function, generated plausible mechanisms, predicted activities from known entities, and predicted entities from known activities while focusing on organization. Their model of molecular explanations was based upon both a literature review and scientific research. They reflected on the work of Adler (1966) and Baker *et al.* (2006) to explain how bacteria move toward chemicals. The model by van Mil *et al.* (2013) represents an explanation of molecular mechanisms based on a scientific

investigation, using the heuristics of entities, activities, and organization from Machamer *et al.* (2000), but the model is based on only one example from biology research.

Some science educators who recognize biology as a science that answers different types of questions have identified a typical difficulty. Students conflate proximate causes (“how”) with ultimate causes (“why”) when explaining biological phenomena (Abrams and Southerland, 2001). In addition to this difficulty, there are several other problematic characteristics of mechanistic explanations. First, unlike facts and procedures, mechanistic explanations are generally hierarchical and often have hidden causes, which produce an illusion of explanatory depth (Rozenblit and Keil, 2002). Likewise, depending on the familiarity of context to the student, student explanations of molecular behavior attribute cause at various levels of depth (Talanquer, 2010), and students often fail to transcend levels of biological organization when constructing explanations about a biological phenomenon (Lewis and Kattmann, 2004; Duncan and Reiser, 2007). Second, mechanisms are often depicted with cartoon diagrams, and students tend to have difficulty relating such visuals to appropriate reasoning about explanations (Schönborn and Anderson, 2009; Anderson *et al.*, 2013; Tibell and Rundgren, 2010). Some reports have found that scientific explanations may blend with everyday explanations, which are often vague, idiosyncratic, intuitive, and anecdotal (Treagust *et al.*, 1999). These everyday explanations may use semantics that address processes as governed by actors that have intentions, such as letting, hindering, and helping (Talmy, 2000). Informal reasoning views processes as happening because actors have intentions and they use their abilities to achieve their purposes. In contrast, biological mechanisms are processes constrained by physical principles in systems at multiple scales from macroscopic to submicroscopic levels.

In addition to the above-mentioned reasons why biological mechanisms may be difficult for students to learn, another problem stems from the current debate as to what constitutes a mechanistic explanation. A mechanistic model is one type of explanation based on identifying the underlying causes of a phenomenon, typically by accounting for the physical entities, including their properties and interactions, and the activities that cause a chain-like change in the organization of the entities and activities across time and space (Braaten and Windschitl, 2011). For example, growth factors signal cells to multiply when their organization and the activities of the underlying molecular entities cause changes. Russ *et al.* (2008) argued that a satisfactory definition of a mechanistic explanation is needed in science education, citing that it is inappropriate to simply characterize mechanistic explanations as nonteleological formulations, simple causal explanations, or descriptions of the underlying structures. There is a need to apply these reports from philosophy and education to learn whether practicing biologists follow a mechanistic model of explanation when they explain molecular and cellular mechanisms in the biological systems they investigate.

In the present study, we approached our research by asking which model most accurately reflects how scientists really explain the biological mechanisms they investigate. Both science educators and authors of curriculum reform documents would benefit from a clear model of how biologists explain molecular and cellular mechanisms. Clearly,

there is agreement that undergraduate students who learn biology are expected to develop skills around explaining mechanisms so that they overcome such difficulties and become more expert in their approach to explaining science. Thus, a model of how biologists explain, if made available, could show students what it means to explain effectively to help them know when they fully understand a biological mechanism.

The purpose of this study was to characterize how experts from different subdisciplines of biology construct explanations about molecular and cellular mechanisms with the ultimate goal of improving student explanatory skills in this area. In so doing, we sought to gain greater insight into the essential aspects of biology experts' explanations of molecular and cellular mechanisms by identifying components that apply to all of their explanations. To do this, we addressed the following specific research questions: 1) What is an appropriate model of the components of explanation used by biology experts to explain molecular and cellular mechanisms? 2) Do explanations made by experts from different biology subdisciplines at a midwestern U.S. research university support the validity of this model?

METHODS

The above research questions were addressed with the modeling process of Justi and Gilbert (2002) as used by Schönborn and Anderson (2009) to guide our entire model-development and validation process. Models, often used in science, are simplified purposeful representations of abstract ideas, complex processes, or phenomena, and modeling is the act of developing a model. Justi and Gilbert (2002) proposed a modeling framework to depict the process of model development as an iterative process containing four stages. Mendonça and Justi (2013) state that this approach to the modeling process provides important insight into both the essential concepts and the logical coherence of reasoning about concepts for scientific thinking.

The stages of modeling and how each stage is addressed in this study are shown in Table 1. Stages 1 and 2 were done to address our RQ1; stage 3 to address RQ2; while stage 4 is dealt with in the final *Discussion* section. Regarding stage

1, we decided that our purpose was to model the essential components of explanation that a biologist includes when explaining a biological mechanism. With this purpose in mind, we formulated an initial mental model based on the research literature on molecular mechanisms, especially the reports by van Mil *et al.* (2013) and Machamer *et al.* (2000). In stage 2, we expressed our model as a range of iterations of verbal and visual models, each time as per stage 3, testing them with various thought experiments and predictions. Stage 3 also involved checking whether the model fulfilled its intended purpose by testing it with empirical evidence from interviews with biologists and further thought experiments to come up with a modified, final model. In stage 4, the usefulness of this model was then evaluated by considering its scope and limitations.

Description of the Initial Mechanistic Model

As described earlier, the initial model was grounded in the work of van Mil *et al.* (2013) and Machamer *et al.* (2000). As a first thought experiment, we considered how the components in the van Mil *et al.* (2013) model fit with explanations for both regulatory mechanisms of physiology and the transcriptional regulatory networks of developmental biology. According to the initial model, expert biologists giving mechanistic explanations identify relevant *entities* for the mechanism (e.g., protein complex, biomolecules, and organelle). Next, they might claim that the *entities* have a specific *state* (e.g., phosphorylated, active, and methylated), which will then undergo a *state* change when the *entity* *interacts*. Experts will proceed to explain how these *states* change and begin talking about *activities*. The explanations may then transition from *activities* back to introducing *entities* in the mechanism, or the experts will begin explaining how the mechanism is *organized*. They will refer to what is happening over *time* (e.g., rates, sequences, and duration), they will describe how *entities* and *activities* are *organized in space* (e.g., orientation, localization, and compartmentalization), or they will switch between the *levels of organization* (e.g., molecular level and cellular level). By shuttling between the three areas—entities, activities, and organization—the expert coherently explains how processes happen in the cell via proximate causes. For a visual representation of this initial model and its application to explain bacterial chemotaxis, see van Mil *et al.* (2013).

Table 1. Stages of the Justi and Gilbert (2002) model of modeling and their use in this study

Stages of modeling	Operations within this study
1. Decide on the purpose and formulate an initial mental model.	The purpose is to model the essential components used by biology experts to explain molecular mechanisms. An initial model, formulated based on the research literature on explanations and molecular mechanisms, was heavily informed by reports from van Mil <i>et al.</i> (2013) and Machamer <i>et al.</i> (2000).
2. Express the mental model with material, visual, verbal, or another mode of representation.	The model was expressed initially through a range of iterations of verbal and visual models.
3. Test the model with thought experiments, predictions, and empirical evidence to see what needs to be modified for it to fulfill its purpose.	Fulfillment of purpose was tested with empirical evidence from interviews with biologists, and the model was further modified to produce the MACH model.
4. Evaluate the scope and limitations of the model.	The usefulness of the MACH model is addressed in the <i>Discussion</i> to evaluate its scope and limitations.

Table 2. Participant research scientists and their various subdisciplines of biology

Pseudonym	Field of study	Laboratory's research question	Experience in years
Darth	Neurobiology	What are the cellular mechanisms that shape auditory processing?	19
Sally	Cancer biology	How does a transcription factor affect cell behavior?	37
Molly	Physiology	How does calcium signal smooth muscle contraction?	12
James	Developmental and cancer biology	How does gene expression affect cell function?	36
Jay	Structural biology and biophysics	How do viruses assemble in a cellular environment?	8
Frank	Neurobiology	How are organelles transported within the axon?	34
Buck	Cancer biology and physiology	How do hormones from fat tissue promote or repress cancer growth?	16

Using a Textbook Explanation to Exemplify the Initial Model

The initial model was then applied to exemplify its usefulness as a tool for analyzing a textbook explanation and a diagram from the textbook *Molecular Cell Biology* (Lodish *et al.*, 2000). For example, figure 20-23 in *Molecular Cell Biology* depicts part of the mechanism that explains how cells “know” how to grow. It shows how epidermal growth factor (an entity) binds (an interaction) to its receptor (an entity), transcending the cell membrane (spatial organization). This binding allows the receptors to dimerize (an activity due to spatial organization). Once the receptors dimerize, the receptors interact and activate each other through an enzymatic phosphorylation reaction (an activity), which causes a conformational change in the dimer (a change in state). With these phosphate groups attached (state), the receptors can recruit (activity) adapter proteins (an entity). The textbook authors continue, “The adapter protein GRB2 binds to a specific phosphotyrosine on the activated RTK [the receptor] and to Sos, which in turn interacts with the inactive Ras • GDP. The guanine nucleotide–exchange factor (GEF) activity of Sos then promotes formation of the active Ras • GTP” (Lodish *et al.*, 2000). These actions create a signal cascade that eventually activates transcription of genes involved in proliferation.

The textbook author’s explanation of this mechanism exemplified the initial model and provided us with a starting point for discussing and exploring other explanations of molecular and cellular mechanisms. Our question (RQ1), though, was whether this model would also represent how expert biology researchers explain mechanisms, or would the approach prove only applicable to textbook author–type explanations? This issue was investigated through interviews with our selected biology experts (RQ2). At the same time, the empirical data from the interviews, as well as our own intuition and thought experiments (Justi and Gilbert, 2002), enabled us to use components of the initial model to develop several modified models for mechanistic explanations in biology (RQ2).

Selection of Participants

Seven biology expert biological research scientists from a large midwestern public research university in the United States were recruited for this study. By studying multiple experts in related but distinct fields of biology, we sought to make explicit those components of their explanations that contain knowledge across the subdisciplines of biology, so that we may find consensus themes across the subdisciplines. Thus, the participants were selected purposefully, based on two criteria used for theoretical sampling (Patton, 2002).

First, the participants had to be faculty members of a biology department who had done research on a molecular or cellular mechanism and had published their findings. Second, the selected biologists had to be from a range of biology subdisciplines that study molecular mechanisms. In this way, a range of biological perspectives from different subdisciplines that deal with molecular mechanisms could be synthesized to inform components of mechanistic explanations that apply to all of their explanations. Table 2 gives biographical information about the participants, including their number of years of research experience, their fields of study, and the research questions they address. Hereafter, we refer to these participants as “biology experts.”

Although the participants represent a variety of subdisciplines, some fields within biology are absent. For instance, researchers of biochemistry, plant biology, computational biology, and other mechanistic fields have been excluded. This is a limitation discussed below. Pseudonyms were used to protect participant identities and research was performed under the approval of the Institutional Review Board (protocol #120301239).

Description of the Interview Protocol

The biology experts participated in semistructured interviews of 50- to 120-min duration. This qualitative approach allowed us to describe in detail and depth how expert biologists explain mechanisms, thereby facilitating the testing of the initial model and subsequent modifications thereof to reach our final model. A major part of the interview involved openly prompting the participants to explain a mechanism of their own choice (modified from Schönborn and Anderson, 2009). The interview commenced with the following guiding statement:

Today I would like you to talk about cellular mechanisms. Take your time and start thinking about these types of processes. Take as much time as you want, don't rush, just relax and think about them for a while. Try to imagine it; mechanisms inside the cell, think about everything you know about *what* these are and *how* they work. Ok, what are you thinking about now? Tell me slowly and clearly. Take your time.

This statement was intended to focus participants on explanations of molecular and cellular mechanisms by prompting them to explain “how” these work rather than “why” they work. Furthermore, each participant was encouraged to explain the mechanism he or she knew best from having extensively studied it in his or her research.

The purpose and methods of the study were made explicit before enrollment in the study. The interviewer was perceived as a fellow biologist (trained in developmental biology) rather than as a student, but not with expertise in the same discipline as the expert who was interviewed. Interviews are dynamic, and the researcher attempted to come to an understanding of the participant's explanatory knowledge by probing to coconstruct shared knowledge during the interview as might happen during a conversation between two scientists. Member checking was integrated into the original script, such that the researcher would repeat back the key points of the expert during the interview, and then the participant researcher would confirm the summary and clarify or expand the explanation (Lincoln and Guba, 1985).

Data Collection and Processing

The data consisted of transcribed audio recordings of the interviews, written notes taken by the interviewer, and drawings and artifacts produced by the respondents during the interview. The transcribed data were analyzed qualitatively using NVivo data analysis software, version 8 (QSR International, 2008). The data set of interest was limited to the sections of the transcripts in which participants provided explanations of a mechanism studied in their research (i.e., background information and other speech not addressing the research question was excluded). Thematic analysis as described by Braun and Clarke (2006) was used to construct themes and patterns that fit the explanations of the experts. Analysis occurred concurrent with data collection, such that interviews continued until the themes reached saturation (Lincoln and Guba, 1985). Additional interview data were redundant after the fifth interview of the seven biology experts, when it was found that the additional interviews were no longer revealing new themes or insights. The themes were reviewed as per Attride-Stirling (2001) by constructing and reconstructing thematic networks with the codes, categories, and themes. These themes provide the evidence for the validation of our final model (RQ2). Once data were collected, multiple colleagues assisted in the analysis of the data during weekly meetings with the coauthors and debriefing meetings with a larger research group. In addition, the participant biologists corroborated findings by reviewing the results of the research report for accuracy and clarity (Lincoln and Guba, 1985). They edited the grammar of their excerpts during a final member-checking session to improve readability from the colloquial transcript; these post hoc edits did not affect the analysis or findings.

RESULTS

Validation of the Initial Model with Expert Explanations from Different Biology Subdisciplines

To address RQ2, we constructed themes from the explanations provided by the biologists. As expected, we found that components included in expert explanations were predicted by the initial model. In addition, though, their explanations also included features not associated with the initial model, leading us to modify it to the final model presented later. Four major themes emanated from our analysis of the transcribed interview data. It was found that our biology

research scientists used the following components when they explained biological mechanisms:

- They used the initial model of mechanistic explanation by focusing on entities, activities, and organization (how theme);
- They highly contextualized and constrained their explanation according to biological and societal significance (context theme);
- They integrated explanations with the methods, instruments, and measurements they use to investigate their mechanism (methods theme); and
- They used narrative stories along with analogies to explain their systems (analogy theme).

The interview data revealed that these themes operate together when biologists construct thorough mechanistic explanations of the systems they investigate. In the following sections, we present supporting empirical data for each of the above themes and show how the different biologists we studied used the strategies and knowledge represented by each theme to do mechanistic thinking. The excerpts below offer representative quotes of each theme. Each of the seven biologists' explanations contained all four themes. These themes allowed us to test and modify the model with empirical evidence toward fulfilling our purpose.

The How Theme: Biologists Focus Explanations on the Entities, Activities, and Organization of the Mechanism. From analysis of the interview transcripts, it was clear that our sample of experts dedicated a significant amount of talk to the mechanism of interacting biological entities. Ubiquitously, the experts refer to what the states of those entities are, how they interact, and how they induce other entities to change states. For example, Sally, a cancer biologist, explained signal transduction via the epidermal growth factor (EGF) pathway. She states,

EGF binds to its receptors and brings them together, the purpose of bringing them together is to activate the receptor kinase domain, so when they come together that they first act on each other to provide the right phosphorylation to activate the kinases. Then, these guys become phosphorylated all over the place, and that forms sites for proteins to dock. Protein X comes on here, protein Y comes on here, ... and that docking obviously provides access to additional signals. (Sally, lines 238–246)

In Sally's explanations, the EGF, receptors, domains, and proteins represented the entities. The receptors changed state by coming together and becoming phosphorylated, which induced the receptors to have activity. In this case, the activity was to change the state of other proteins. Note that this molecular level explanation used terms like "dock" and "bind" to describe the interactions. This analysis was strengthened by the diagram made by Sally while explaining the EGF pathway (Figure 1A). A focus on these parts of the initial model was common among the biologists we interviewed, and explanations included how the activities and entities were organized.

Consistent with the initial model, the experts integrated their explanations of entities and activities around three

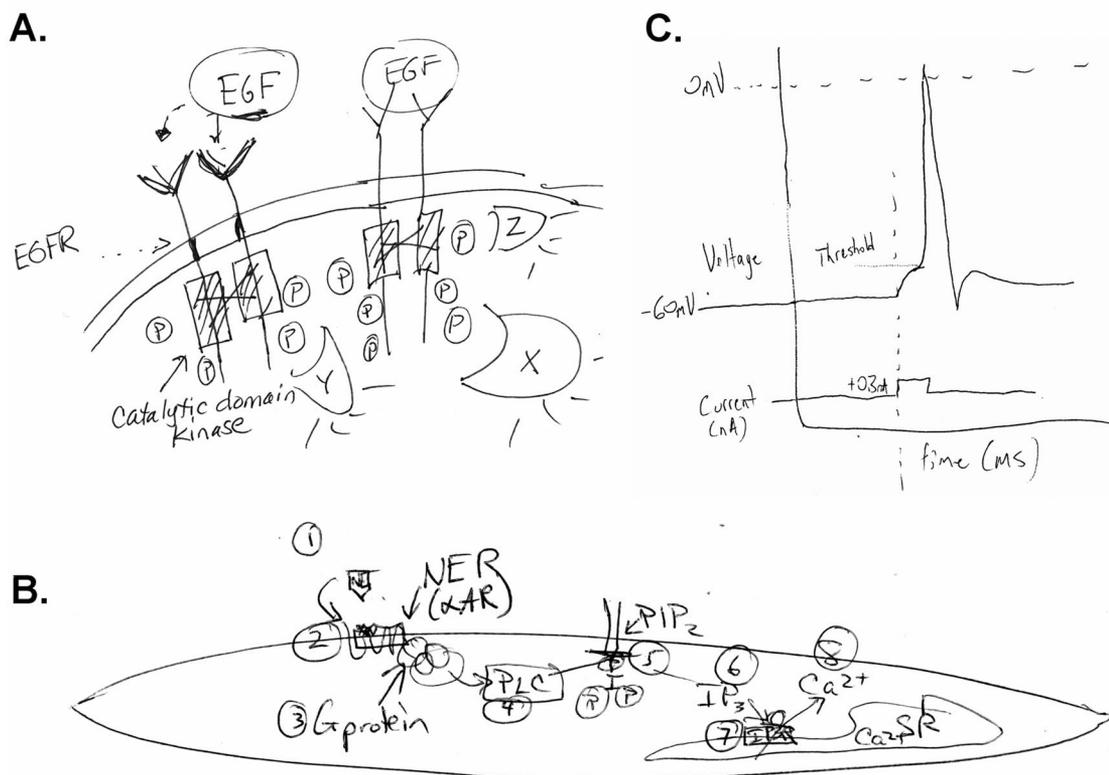


Figure 1. These illustrations are typical of drawings made by scientists as they explained a mechanism they investigate. Panel A shows a diagram of the EGF signaling mechanism by Sally indicating a model of signal transduction that plays a role in cancer. Panel B shows a schematic diagram by Molly of the mechanism that releases calcium to regulate contraction of a vascular smooth muscle cell. Panel C is a graph by Darth displaying the mechanism of an action potential of a neuron.

types of organization of their chosen systems. Temporal organization, spatial organization, and the multiple levels of biological organization were important considerations to the experts both implicitly and explicitly. For example, as a structural biologist, Jay explained the system with which he works (i.e., viral assembly):

Very specific reactions are occurring at specific locations, and as we look at higher and higher resolution, these chemical reactions can only occur if their concentrations are driven up in specific areas. I often think of this like real estate that is the location is the key, ... the biological chemicals need to be at the proper spot, and they have to be there at the right time, so it is this really coordinated event. [It] is not actually three-dimensional. [It] is four-dimensional; you have timing and location, all come together for these events to occur. You don't want RNA to come off of here and go throughout the cell because you know that could be wasted energy it may not find coat protein. Viruses don't want to waste energy just like the cell doesn't waste energy. (Jay, lines 312–325)

In Jay's explanation, there was a specific focus beyond just the "biological chemicals," which is to say the entities. Jay pointed out that "location" and "timing" drive biological events. Succinctly, Jay proclaimed, "It is this really coordinated event. [It] is not actually three-dimensional. [It] is four dimensional." Both spatial and temporal organizations were distinct as aspects of mechanistic explanations.

Explanations from our participants commonly discussed temporal organization. For instance, Molly extrapolated on the mechanism of how norepinephrine signals lead to the shortening of vascular smooth muscle cells when asked to draw her internal representation (Figure 1B).

Molly: Here is my G protein coupled receptor which is a seven transmembrane receptor. Here is the G protein. Here is norepinephrine, so it binds there [the receptor]. Here is phospholipase C, this comes off and binds there, phospholipase C then cleaves off this I with a phosphate here, a phosphate here, and a phosphate there, it cuts here and then you get this IP₃. The SR [sarcoplasmic reticulum] has calcium inside. And then here is the IP₃ receptor so when IP₃ comes across and binds here calcium comes out.

Interviewer: And what do those arrows represent?

Molly (while numbering diagram): The sequence of time. Therefore, it is basically, here is the first step, ... the rise [in] norepinephrine. Here is the second step binding to the alpha androgenic receptor and here is the third step the G protein gets activated, and then here is the fourth step. It is phospholipase C becomes activated. And here is the fifth step. It would be cleavage of IP₃. (Molly, lines 167–184)

As before with Sally, Molly used entities, interactions, and activities, but this explanation also considered temporal

organizations. Molly used the diagram of norepinephrine's action to represent the sequence of events symbolically. The "arrows" of the schematic diagram represented steps in time, rather than precise spatial movements. Temporal organization was a key part of both the excerpts from Jay and Molly, and these were representative of the other experts as well, who also considered time and space as two of the three ways mechanisms are organized.

A third way our experts considered organization was across multiple levels of organization. The developmental biologist, James, explained the function of secretory cells in the pancreas:

We work on cells called pancreatic acinar cells and these cells secrete digestive enzymes. To accomplish this they have to maintain a cell polarity, where they have a distinct apical and basal boundary and intracellular organization of organelles so that they synthesize the protein at the correct location. At the apical surface are granules called zymogen granules that package the digestive enzymes, so when you eat, you get a signal from a hormone, known as CCK, cholecystokinin, that binds to a receptor that is on the basal surface of these cells. There is a calcium wave that goes through a complex signaling cascade, but eventually these little zymogen granules fuse with the plasma membrane and therefore release their digestive enzymes. And then those digestive enzymes go through a duct system, ... that comes out into what is known as the pancreatic duct and that feeds into the intestines. (James, lines 75–89)

James explained his chosen system lucidly and readily translated vertically (Schönborn and Bögeholz, 2009) between many levels of biological organization. He began with cells, zoomed down to the organelles, then molecules (i.e., enzymes). After the molecules, he identified zymogen granules, which are cell structures, and then zoomed out from the receptors, to the pancreatic ducts and organs. This kind of transcending explanation was typical throughout the interviews with the biology experts, who without hesitation readily translated through different orders of biological organization and scale when discussing their mechanisms. To answer RQ2, overall, the initial model captured each of our participants' explanations, since there was pervasive use of entities, activities, and organization by the participants, thereby confirming the representation by van Mil *et al.* (2013) and supporting the fact that these components should be retained as part of any modified model. However, the results from our interviews also revealed several other notable themes, which allowed us to significantly modify our initial model to better represent the explanations used by experts in this area.

The Context Theme: Biologists Contextualize Explanations by Considering Biological and Social Relevance. The initial mechanism model did not capture the great deal of contextualizing that experts exhibited. We found that the biologists we interviewed always considered a context in their mechanistic explanations. That is, they considered the biological systems they explain. This is because mechanisms are rooted in the cell type, organism, evolutionary history, and other biological contexts. For instance, Sally observed, "These signals (growth factors) ... go and tell the other organelles what to

do in response to the signal, and that is what varies from cell to cell" (Sally, lines 247–249). She qualified her explanations to emphasize that the mechanism varies depending on the cellular context. Furthermore, Frank, a neurobiologist, explained his laboratory's system of choice:

You can mutate or knockout in a fly the same gene that gives a human who has that gene mutated or knocked out a specific disorder. We work with flies that have the same mutation in the frataxin gene as humans with Friedreich's ataxia. Now [we are] working with flies that have the same mutations in the parkin or pink1 genes that people with hereditary Parkinson's disease do. Now it is not that a fly [is a] great model for a human being getting Parkinson's disease. It is that we are looking at what happens at the cellular level. It's about what is the cellular neuropathology in a neuron in an intact nervous system, even if it is a fly. (Frank, lines 111–116).

Frank distinguished several contexts in this excerpt. First, he pointed out which organism his lab uses, *Drosophila* (fruit fly), and justified its use as a model organism to understand another organism, namely humans. Second, his explanation related to the broader context of human health, to the disorders he wished to understand, namely Parkinson's disease and Friedreich's ataxia. Finally, Frank's explanation returned to the cell type being used by stating, "the cellular neuropathology in a neuron." Thus, both the biological context of the mechanism and its context in society were associated with the biologists' explanations. Overall, the research scientists' explanations featured highly contextualized mechanisms, suggesting that context was an important component of our modified model.

The Methods Theme: Biologists Insinuate Explanations with the Tools, Methods, and Measurements of How They Know. A ubiquitous characteristic of the explanations that we obtained from the participant biologists was a consistent reference to methods they use in their respective laboratories. The biologists contextualized the mechanisms they explained by the methods, tools, and practices they use to generate the data that inform their mechanisms. Darth's explanation of action potentials illustrated just how entangled instrumentation and explanation were. He went into great depth while explaining the sequence of ion channels opening during an action potential and drew a graph to represent the phenomenon (Figure 1C). Darth, a neuroscientist, explained,

I've recorded these in a lot of different ways, so I can also imagine an oscilloscope trace, and also in vivo, the extracellular trace. ... This would be what an electrode sees if you recorded intracellularly, so let's say with a patch clamp electrode, but often with our metal microelectrodes, we record action potentials extracellular[ly] and then they have a different waveform. (Darth, lines 552–556)

Darth's explanation considered the electrodes, oscilloscope, placement, and type of sample (in vivo vs. in vitro). Furthermore, Darth's graph was how he visualizes the mechanism, not as a schematic model but grounded in the techniques and instruments used in his lab. His thoughts about what the mechanism is and how we know the mechanism were inseparable. This trend of focusing on measurements

and laboratory practices was also well articulated by Frank on the topic of organelle movement in the synapse. He reflected,

Some people would say that all the mitochondria headed for the synapse, they go $0.35 \mu\text{m/s}$... At the synapse, which needs mitochondria to arrive there, it cannot tell how they got there. ... To be teleological, all the synapse cares about is how many cross this line per unit time. So often we find that flux measures, just putting a mark down and saying how many mitochondria cross that line ... per unit time, that sometimes is the most interesting thing, because that obviously integrates how fast they are moving and how much of the time they move. (Frank, lines 372–379)

Frank's constructed explanations took into account the limitations and strengths of different methods. For him, understanding the activity of the mitochondria in the neuron was intimately related to the way the measurements were taken. Measuring flux was Frank's way of combining the activity and spatial organization of the axonal transport mechanism. The excerpts represent the tight linkage between the explanation and methodology used in the experts' laboratory practices, suggesting that this aspect would be an important component of any modified model.

The Analogy Theme: Biologists Use Stories and Analogies when Explaining Mechanisms. Within each explanation, we found that the biologists that we interviewed used narrative forms along with scientific models and analogies. The use of representations, a type of analogy (Clement, 1988), is evident in the artifacts of the participants; Figure 1, A and B, shows schematic diagrams that were typically seen with mechanistic explanations. Molly used scientific models to structure her explanation and was able to consider the limitations. She states, "I know the model is flawed because I can think of data that raises questions about parts of the model" (Molly, lines 86–87). Molly connected her model of norepinephrine's action to the data.

Scientific models were not the only way biologists made sense of explanations. The participants also used other analogies in their explanations; these analogies communicated their knowledge about the submicroscopic world. For instance, Jay highlighted that the research that has been done before "would kind of be like watching a car be put together but outside of the factory" (Jay, line 203). Jay communicated the distinction of studying a system *in vivo* versus *in vitro* using a factory assembly analogy. There were also many other analogies used in a variety of ways. For instance, James communicated the concept of modularity of biomolecules using a popular toy as an analogical model by stating:

We can take two proteins. I can take the DNA-binding domain of one protein and put it on another protein and that DNA-binding domain will work. To me, that is unbelievable. I just take a chunk of amino acids, of protein, and stick it on this ... and it works. It is like Mr. Potato Head. You can stick on the arm of Mrs. Potato Head, and it works. (James, lines 389–394)

Making analogies was clearly a creative way our biology participants adorned their explanations, and it often helped them illustrate the links between the molecular world and the macroscopic world.

Surprisingly, participants also used teleological and anthropomorphic formulations and more general narrative stories to explain molecular and cellular mechanisms. By "teleological formulation" we mean backward causation. For instance, the explanation may focus on the end result of the mechanism, the purpose, or needs (see Zohar and Ginossar, 1998). Among the analogies used, our experts attributed human characteristics to nonhuman objects, which is to say they anthropomorphized the mechanism (see Zohar and Ginossar, 1998). For instance, Jay introduced the purpose of his research by explaining:

[With a] segmented genome, the virus needs to know the virus has three [DNA] segments. It has to somehow determine that it has packaged all three segments to form an infectious virus. So somehow, viruses have developed a mechanism for counting, which is interesting at the structural level. This virus can go, "Yep, got them, all three. Okay, we are ready to leave the cell." (Jay, lines 189–192)

Jay and many of the other scientists assigned anthropomorphic actions to their entities during the explanation. In this case, Jay used both. He first focused on the purpose of viral assembly, and then he attributed the viruses with the ability to "know" and to "count." Teleological statements are also common in other explanations. For instance, Frank explained, "You have most of the mitochondria stationary ... they're piled up at nodes of Ranvier where you have all this ion pumping, and guess what, you need a lot of ATP. That sort of makes the kind of common sense in a way. ... Put it where you need that function" (Frank, lines 195–200). In Frank's case, the organization and activity of the mitochondria were extremely important for other functions. The "common sense" to which he was referring is the idea that the needs of the system helped him make sense of what components will be used. We expand on this later during the final discussion.

The interviews and analysis showed that narrative forms of explanations, including the use of teleological reasoning and anthropomorphic characteristics, were present in the explanations of our participant researchers, accompanied by analogies and scientific models. These findings suggested the importance of including these aspects of explanation in our final model.

Exceptions within Themes. While thematic analysis can capture succinct ideas from the data, the themes may overlook unique cases and disconfirming evidence. This section elaborates on data that did not fit the previously discussed themes but yielded important insights worthy of noting.

Explanations gave variable emphasis to some feature of our initial model. First, most biologists associated activities with state changes; these typically meant a chemical or conformational change to a protein or other property and entity. State changes involved changes in both space and in time. However, Jay, the structural biologist, infrequently described temporal changes in state, instead focusing much of his explanation on spatial features at the molecular level. When Jay discussed protein interactions involving the structure and position of viral assembly, he did this in terms of their orientation and location. He states, "They have to be there at the right time" (Jay, line 321). Based on information

about location, a temporal sequence was inferred. Thus, activities (e.g., turning off and on) did not characterize his explanation; the entities did not change in this way. Rather, the entities changed through spatial organization, by stages of assembly. In contrast, Sally ignores molecular location and orientation when she states, “these guys become phosphorylated all over the place.” Instead, Sally emphasizes the temporal sequence of events when she states, “they first ... activate the kinases” (Sally, lines 240–241). We attributed this difference in their explanations to the fact that Sally, as a cancer researcher, has a different perspective from the structural focus Jay uses as a researcher. Changes in entities and organization were included to different degrees when the participant biologists’ explanations were compared with the initial model.

Second, we noted that our interviewees used levels of organization in different ways. Jay, for example, remained primarily at the molecular level, while Sally explained across multiple levels but did not envision the molecular scale. For instance, she stated, “I don’t see any carbon bonds anywhere, even DNA. I don’t see [a] carbon bond. I just see a double helix. I don’t see bases or anything, I would just see a helix” (Sally, lines 388–389). Sally also did not imagine movement at the molecule’s timescale. However, Sally’s explanations integrated organization at the higher levels. For her research program, thinking about intramolecular features was not useful. These observations point out that some of our biologists prefer a particular level of organization. The researchers found a particular level useful for their particular research questions. These results suggest that the initial model will not perfectly represent experts’ explanations; emphases for the components varied in explanations from diverse experts. The components (i.e., themes) are present but at different depths and with some degree of flexibility.

Third, within the theme of context, societal contextualization gained the least support compared with biological context. While each participant drew connections to the societal significance of, for example, knowledge of disease, this happened infrequently (one to three times per participant) compared with the biological context of the theme. This finding is understandable; most scientists would be expected to focus more on their immediate context (e.g., the organism) than that of broader context areas (e.g., human health) when generating an explanation.

Fourth, regarding the analogies and narrative forms of explanation, some of our interviewees used metaphors that were unscientific in nature. When using teleological and anthropomorphic explanations, they would often point out the limitations of their thinking. For example, James used the term “know” when describing the cell in general and, when asked to elaborate, stated the following:

James: This [replication] machinery is very complicated. The cell has to bring in the correct ribonucleotide. It has to *know* that the next one should be an A, and not a U, not a G, not C, but an A, so it has to *know* that. It has to figure that out. Knowing is probably not the right term but it has to figure it out how to make sure the right ones there. Then it has to be ligated ...

Interviewer: You used the term “know” and then you corrected yourself ...

James: I don’t think cells think like we do, and I do that all the time, I catch myself saying that all the time in the classroom. ... I like to talk about cells like they are people, you know like they have personalities. We actually use those terms in the lab all the time to say our cells look good. You know it is not very scientific. Are they smiling at you today? When you look under the microscope, they look good, but that is not a very precise scientific term and I often will say things like they have to *know* when to divide, you have to *know* when to differentiate. (James, lines 192–217)

James emphasized that, even though he used anthropomorphic characteristics to describe cells, he was not doing so in a “scientific” way. This language was in his lab and in the classroom. He pointed out that there are different levels of precision that the explanation can provide. This example shows us that the biologists’ explanations contain ways of telling their story that are less precise versions of mechanistic explanations. In conclusion, we discovered from the data that there were clear variations between individual biologists in how our participant sample used the various aspects of explanation. This is not surprising, given the intrinsic differences between the biology subdisciplines and the variation between humans.

Modifying the Initial Model into a Final Model: Fulfilling the Purpose of the Model

To summarize, the empirical data obtained from biology experts at one midwestern U.S. research university led to our identification of the following four major themes composing their explanations about molecular and cellular mechanisms:

- Our participant biologists acknowledged limitations to the mechanism based on how they learned about it using tools, measures, and methods (methods theme);
- They explained why the mechanism happens through a story or analogy (analogy theme);
- They contextualized their explanation to show how it was useful (context theme); and
- They explained how the mechanism works by identifying entities and their activities and organization (how theme).

These identified themes permitted us to look at the initial model with “new eyes.” First, we realized that the initial model corresponded to the how theme and was, therefore, a valid component of expert explanation. Indeed, the initial model foretold a substantial amount of the explanation provided by the experts in that interacting entities, activities, and organization are important aspects of molecular and cellular mechanisms. The interviewed experts explained what the states of the entities are, how they interact, how the entities and activities are organized in time and space, and what the relationships are across multiple levels of organization. Second, we realized that the initial model did not accommodate our other three themes. This observation informed the decision to modify the initial model into a final model, which we term the “MACH model” (Figure 2). In our view, this model, with its four components, shows how the themes fit together when experts formulate a complete explanation of molecular and cellular events. In view of the interactive nature of the four components of the MACH model,

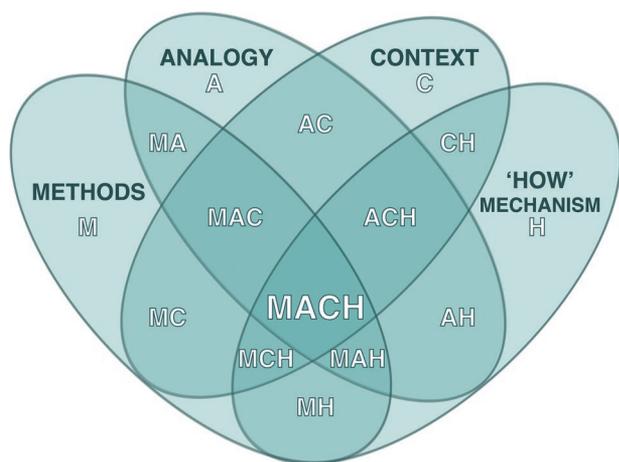


Figure 2. The MACH model of explanations. A Venn diagram representing the components of explanations based on themes from interviews with research scientists: the Methods, the Analogy, the Context, and the “How” of the mechanism. In this study, all of the biologists’ explanations are represented by MACH and contain all of the components.

in that explanations can compose a range of combinations of component factors, we considered several possible ways of representing this model but, for multiple reasons, finally settled on a Venn diagram. Venn logic, which is based on set theory, conveniently illustrates how, for example, experts not only explain mechanisms according to the “how” (H component in Figure 2) theme (as per the initial model) but also ground their explanations in methods (M component), analogies (A component), and the various contexts (C component) of relevance to the particular mechanism. In Table 3, we propose operational definitions for the components of the MACH model. The Venn diagram and definitions of the MACH model serves as a representation of the components biologists from various subdisciplines consider when they explain molecular and cellular mechanisms.

CONCLUSION AND DISCUSSION

In this project, we addressed the following research questions: 1) What is an appropriate model of the components

of explanation used by biology experts to explain molecular and cellular mechanisms? 2) Do explanations made by experts from different biology subdisciplines at a midwestern U.S. research university support the validity of this model? Findings presented in this paper suggest that we have indeed developed and validated an appropriate model of explanations made by biologists who investigate molecular and cellular mechanisms at one midwestern U.S. research university and thereby achieved the purpose of the modeling process defined by Justi and Gilbert (2002). Building upon the mechanistic model of explanations by van Mil *et al.* (2013), the MACH model brings refreshing clarity to what it means to explain “how” in biology.

Our analysis suggests that there was a high amount of contextualization when explaining biology (context theme). As seen in other research examining expertise in other disciplines (e.g., Chi, 2006), research scientists qualify and constrain the extent of generalization and focus more narrowly on specific contexts. Indeed, our biologists demonstrated that explanations have limits, and these limits revolve around biological context and relevance to society. Repeated and interwoven references to methods, data, and instruments that have informed the mechanism are another way that our biology experts imposed conditions or limits to their explanations (methods theme). Our participant biologists all grounded their explanations in the types of questions their labs are asking and the tools used in their research to answer these questions. The variety of methods used by the scientists of different subdisciplines in our study gave the explanations different flavors. For example, the structural biologists explained the molecular interactions within the mechanism of interest, but the cancer biologist did not. For the structural biologist, a sequence in time for building viruses in a cell is based on spatial distribution data for particular types of molecules. Thinking about temporal sequence is more useful than thinking about locating molecular interactions for the type of research the cancer biologist does. Constructing explanations around their instrumentation and laboratory settings comes from their extended experience and practice as biology researchers, which is to say their domain-specific expertise. Thus, different methods utilized in mechanism research produce different explanations of mechanisms. Our work shows that explanations interweave with and are inseparable from the practices of life scientists.

Another point worth consideration is the use of analogies. Previously, Clement (1988) reported that scientists, when

Table 3. Operational definitions of the four MACH model components

Component	Symbol	Operational definition
Methods of research	M	The tools (e.g., instruments and devices), data (e.g., measurements and instrument readings), or procedures (e.g., methods, protocols, and techniques) used to generate evidence that informs the explanation and qualifies or limits the generalizability of interpretations.
Analogies and stories	A	The stories and analogies that make sense of and relate to a purpose for the mechanism with formal analogies, models (e.g., representations, diagrams, graphs, etc.), or narrative forms (e.g., teleological and anthropomorphic statements).
Social or biological context	C	The biological context (e.g., a specific cell, tissue or organ type, groups of organisms and their evolutionary history) or social concerns (including human health and disease) that connect the explanation to a setting where it can be fully applied and understood.
How the mechanism works	H	How the component entities of a biological phenomenon interact at the molecular, microscopic, and macroscopic levels to produce detectable changes in state, activities, and spatial and temporal organization.

they solve physics problems, spontaneously create analogies. Findings reported here confirm the notion that expert scientists use analogies (analogy theme), in this case, when explaining the changing activities and organization of entities for their mechanisms. Additionally, scientists in our study used scientific models as a type of analogy (Duit, 1991; Grosslight *et al.*, 1991). Scientific models allow life scientists to focus their explanations on a few components and the organization of those components (as Molly exemplified). The stories and analogies used by experts allow them to structure explanations effectively and, as Frank observed, find the “common sense” in the information. The fact that our experts were using analogies suggests we should not dismiss these types of explanations as unscientific.

Some of our experts combined the “why” with the “how” in their explanations. They considered the ultimate purpose when they explained how their mechanisms work. This was apparent in their use of two other types of analogies, anthropomorphic and teleological statements, which were used in an attempt to provide reasons as part of an explanation. In considering how biologists’ explanations intermingle proximate causes with ultimate causes, it should be noted that this has also been seen with students at many age levels (Abrams and Southerland, 2001). Garvin-Doxas and Klymkowsky (2008) found that many undergraduate students explain biological processes using directed actions, resulting in explanations that resemble backward causation. In other words, when students overlook the role of randomness in a multitude of biological processes, they focus on the benefits of the effect and not the cause. Rather than being wrong and a hindrance to learning, the findings reported here support the idea that teleological and anthropomorphic explanations are less precise explanations used even by experts who can provide full mechanistic details. Treagust *et al.* (1999) suggested that anthropomorphism, teleology, analogy, and metaphor are pedagogical tools for explaining. Zohar and Ginossar (1998) reported that teleological and anthropomorphic arguments had useful heuristic value for learners, and students were able to distinguish between causal and less precise formulations, which is precisely what James did when he said, “I like to talk about cells like they are people, you know like they have personalities ... you know it is not very scientific.” In this sense, the scientist used informal language to explain the biological mechanism as if it were caused by an actor with needs and purposes. Analogical diagrams or stories were used to explain how needs were met to achieve the purposes for the mechanisms the scientists described (Talmy, 2000). In light of the final model, the fact that students explain biological processes using directed actions is consistent with what experts do when they create analogies and formulations to help explain a sequential story around biological functions, purposes, and outcomes.

The multicomponent nature of the MACH model allows for partial explanations that do not constitute all the components of the model. Thus, it will be possible to test the efficacy of this framework beyond our experts to other experts in biology and other sciences and particularly to students, who are less likely to use such complex explanations when discussing mechanisms. The MACH model could also be used to account for variation in sequence and integration of the four components and also which facets of explanation are receiving greater emphasis. The model highlights and

alerts one to implicit components even if they are not woven into an explanation.

Limitations

As with all research, the findings presented here have limitations. First, we must highlight the nature of our sampling. Data were collected only from biologists who investigate molecular and cellular mechanisms at a single midwestern U.S. research university. The MACH model currently only applies to the explanations of molecular and cellular mechanisms from the experts in our study. Different methodologies would be required to generalize the ideas presented herein to all life scientists. For example, several subdiscipline fields that work with mechanisms were not included in our study. Plant biology, biochemistry, microbiology, or systems biology may explain their systems with insightful approaches that may be dissimilar. As another example to indicate limits for the scope of our findings, our data do not allow us to learn whether social context was mentioned by our experts due to influences from their funding situation, since all participants in our study have attempted to convince funding agencies with grant proposals to support their research. Because of the sampling limitations, the model still needs to be tested to understand whether it applies to explanations made by other biologists, including scientists in industry and those from diverse cultures, or to determine how the model would work when viewed from a feminist perspective. Thus, further research is required with wider audiences to understand the implications of this work for science education (Gilbert *et al.*, 1998). Our focus on the content of explanations made by seven participants who are research scientists is only the first step for a larger study to examine how the MACH model might inform learning in biology classrooms.

Thematic analysis also has limitations, one of which is overlooking individual differences. We attempted to analyze some of the deviant instances, but further qualitative research on mechanistic explanations would be fruitful to explore all the possible flavors of explanation, including those that occur rarely. However, the semistructured interview process used here could easily be adapted to study variation among biologists. Furthermore, thematic analysis would not be the best way to learn how the MACH model relates to other models of scientific explanations commonly used in education (Braaten and Windschitl, 2011). As such, future research could focus on testing and clarifying other models of explanation by modeling and interviewing experts who use such explanations. First, some explanations follow a law-oriented model, as summarized by Braaten and Windschitl (2011), which explains by deduction and appealing to predictable patterns, such as the laws of nature. For instance, Mendel explained patterns for inheritance of traits with his laws long before much was known about meiosis. Second, a statistical model of probable factors that predict an observable phenomenon under specific conditions is a model used in education, according to Braaten and Windschitl (2011). For example, epidemiologists explain how factors, such as the frequency of smoking, can affect the likelihood of an outcome, such as a cancer diagnosis. As a third model of explanations, some scientists strive for a unification model that can address the maximal number of observable facts. It is difficult to imagine a unified theory of explanations, but when an electrophysiologist links the opening probability

of a channel at a particular voltage to the measured membrane potential and action potential response in a neuron, the electrophysiology explanation is connecting otherwise disconnected phenomena in a way that is analogous to Maxwell's work, which unified electricity and magnetism to address observations spanning many spatial scales. Future research would benefit from testing these models with interviews to account for how scientists in the biology disciplines explain. In so doing, researchers may adopt the methodology presented here to develop new models for other types of scientific explanations or in other fields.

Finally, as with all models, the MACH Venn model has limitations. Its purpose is to represent how the component themes interact to create coherent explanations. It does not represent, nor is it intended to represent, a process model that would try to indicate the sequence of usage of each component over time. Indeed, there is probably no single logical sequence to including the model components in an explanation. This will depend upon the individual and his or her interests and explanatory style. Another limitation of the MACH model is that, on its own, it does not delve deeply into the specifics of the MACH components that are active areas of science education research. For example, some have argued that use of everyday language and analogies, as distinct from scientific explanations, should be considered when designing pedagogical tools to help students relate science to more informal ways of communication (Treagust *et al.*, 1999). Others have explored the importance of context for learning in biology (Watkins and Elby, 2013). Whether or not MACH helps educators to integrate such different research findings into classroom practice remains to be determined.

Implications

We hope that the outcomes of this research will be instrumental in realizing the recommendations from *Vision and Change* (AAAS, 2011), that is to say, to engage students in formulating and evaluating explanations in a way that is congruent with the practices of scientists.

Future research will focus on exploring the potential usefulness of the MACH model for educators. In this regard, for a previously published model (Schönborn and Anderson, 2009), a range of useful applications were subsequently published (Anderson *et al.*, 2013) that we believe could also be useful applications for our MACH model. For the practitioner, these could include using the model to guide 1) the design of assessments that require mechanistic explanation; 2) the development of rubrics to assess student answers; 3) the identification of student competencies, deficiencies, and difficulties in certain aspects of mechanistic explanation; and 4) the design of class activities and instructional strategies to address such difficulties when teaching students about mechanistic explanations. We have begun to use the MACH model in an educational setting. However, factors such as the explainer, the audience, the content, the educational context, and the culture should be considered before transitioning the MACH model to a classroom setting (Gilbert *et al.*, 1998; Treagust *et al.*, 1999). Instructional activities and a modified MACH model can be found at the Purdue International Biology Education Research Group (PIBERG) ePubs collection (Trujillo *et al.*, 2014a,b).

Table 4. Possible guidelines for transitioning explanations about molecular and cellular mechanisms with the MACH model components into the classroom

Is your explanation robust? Does it ...	
M.	Consider the tools and data used to generate and evaluate the explanation—methods?
A.1.	Make use of appropriate analogies and models—analogy?
A.2.	Tell a story as a narration that makes sense and relates to a purpose—story?
C.1.	Identify a context for the mechanism in terms of organisms or cell types in which it can be fully applied and understood—context of biology?
C.2.	Relate the mechanism to personal or social concerns—context of society?
H.1.	Consider entities, their interactions, and their states or variable properties—“how” of entities?
H.2.	Include changing states of entities to produce activities—“how” of activities?
H.3.	Translate vertically to consider several levels of biological organization—“how” of organization?
H.4.	Translate horizontally to consider spatial and temporal changes—“how” of organization?

Toward the above goals, we have summarized the many observations of this research into a convenient set of guidelines that scaffold the important elements used in a biological explanation (Table 4). These guidelines repeat each of the essential components that were contained in our biologists' most well-investigated systems so that a complete explanation can be provided. Along with the model, we hope that these guidelines can be used in a variety of ways to benefit instructors, students, scientists, authors, bloggers, journalists, and education researchers. We believe this can be helpful for a variety of tasks, including structuring lectures, student self-study (Chi *et al.*, 1994), student peer instruction (Mazur and Hilborn, 1997), communicating with the public, writing and reading textbook or news explanations, assessing student explanations, and providing a theoretical foundation for future work in learning research. The MACH model provides a fresh lens to reinterpret the documented difficulties faced by students. For instance, an explanation indicating a difficulty with transcending levels of organization (Lewis and Kattmann, 2004; Duncan and Reiser, 2007) would correspond to the “H” component. Inappropriate connections to a visual representation (Schönborn and Anderson, 2009) would correspond to the “A” component. Indeed our confidence in the MACH model's usefulness for analyzing textbook explanations was reinforced when we returned to the textbook explanation of the signaling cascade presented in *Molecular Cell Biology* (Lodish *et al.*, 2000) with our new model in mind to find that it not only met the requirements of the initial model but also all components of our final MACH model.

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