THE EFFECTS OF TRAINING BACKGROUND AND DESIGN TOOLS ON MULTI-LEVEL BIOSYSTEMS DESIGN

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Abstract

Biotechnologies could promote healthier lives through advancements such as complex multi-level muscle tissues. Here, cognitive processes among mechanics experts, physiology experts, and novices were investigated to determine what types of knowledge and training are beneficial. An initial hypothesis proposed that domain knowledge is not sufficient for predicting how system redesign affects performance, which was supported by all populations performing poorly on muscle redesign questions; mechanics experts outperformed other populations on force-related questions. A second hypothesis suggested that learning with multi-level design interfaces could aid participants in system redesign, which was supported by all populations performing well after training. A final hypothesis proposed that experts would excel in describing redesign effects, which was supported by expert populations describing more higher-level effects than novices, and the physiology experts suggesting the most effects on patient health. This study lays the foundation for investigating medicine and engineering in design, which has great potential for improving patient health with novel products.

Keywords: Complexity, Biomedical, Cognition, Software, Learning

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1 INTRODUCTION AND MOTIVATION

Emerging intersections in engineering and medicine have great potential for developing novel products for improved patient health (Korin et al., 2012). In particular, additive manufacturing (Giannatsis and Dedoussis, 2009) approaches could enable the production of tailored treatments for personalized medicine (Hamburg and Collins, 2010), such as biologically-based nanomedicine or bioprinted organs (Mironov et al., 2011). The design space for products that utilize biological components is complex and challenging, as biological systems often have many layers of non-obvious emergent behaviors that are difficult for humans to understand and predict (Egan et al., 2013). In this paper, multi-level muscle design is utilized as an example case to determine how designers can effectively understand, learn, and reason about multi-leveled design space, with empirical support from cognitive studies. A multi-level design graphical user interface (GUI) was created to investigate participant learning of system relationships, based on past findings that domain knowledge and inter-level causal reasoning improve human searches of biological systems with emergent behavior (Egan et al., 2015a). Findings from this study seek to promote effective ways for designers to approach complex multi-level systems, which may enable many new products and exciting opportunities at the intersections of engineering and medicine.

Multi-level muscle systems were chosen as a representative system because they exhibit characteristics general to complex biological systems, such as having many parts and scales with layered emergent behaviors (Egan et al., 2013). The layered emergent behaviors are a result of a muscle's hierarchical organization, where discrete levels of organized structures (Fig. 1) interact across scales to power a single muscle contraction.

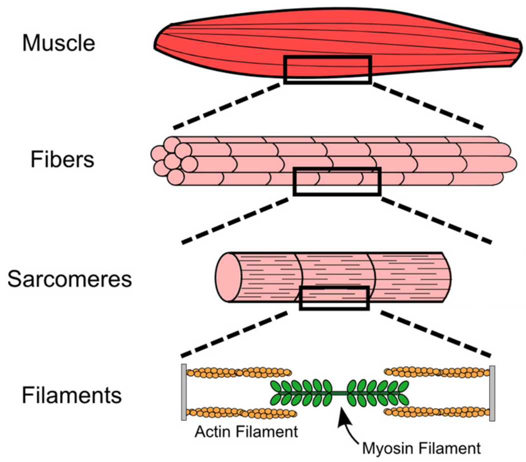


Figure 1. Multi-level muscle organization, from nano- (myosin) to macroscales (muscle)

In Figure 1, one complete muscle (highest level or organization at the macroscale), is sub-divided by fibers situated in-parallel (second highest level) that run longitudinally the entire length of the muscle. Each fiber consists of in-series sarcomeres (second lowest level) that each contain interlaced myosin and actin filaments (lowest level). Myosins are motor proteins that aggregate to form thick filaments, such that all myosins are anchored together and have heads that interact with actin filaments. At the filament level, each individual myosin autonomously and stochastically attaches to an actin filament, exerts force that translates the filament, and then detaches. Actin filaments are anchored to disc-like structures that connect each of the in-series sarcomeres. Through the collective stochastic interactions of myosin and actin within a sarcomere, sarcomeres begin contracting, and through the collective contractions of many sarcomeres, the entire muscle contracts.

Although the emergent layers in muscles may seem highly redundant—a muscle contracts because it's made up of sub-units that contract—myosins operate on fundamentally different principles. Myosins do not contract; instead, they cycle. It is only through their collective behaviors that a qualitatively distinct behavior of contraction emerges. Past cognitive studies have demonstrated that emergent systems with qualitatively distinct behaviors are challenging to understand, but graphical user interface (GUI) aids can aid in human understanding of such systems (Chi et al., 2012). However, few studies have investigated how the understanding of multi-level emergent systems relates to a designer's ability to configure them effectively (Egan et al., 2015a), which motivates the need for testing what types of understanding translate to effective complex systems design, and how GUIs can aid in bolstering beneficial forms of understanding.

Cognitive studies have demonstrated that a person's understanding of complex systems differs in biological domains depending on past expertise and training (Hmelo-Silver et al., 2007), which could affect their ability to design. For instance, in aquarium systems, experts typically have more knowledge of structures and behaviors than novices, which leads to improved understanding and reasoning about interactions within a system. Similar differences in structural and behavioral knowledge were demonstrated among novices and experts for physiological systems related to breathing. Generalist experts, such as academics, were shown to categorize their knowledge differently than other experts, such as hobbyists, which suggests that different trainings could also influence effective design reasoning.

However, these studies did not test whether increased structural and behavioral knowledge was sufficient for correctly reasoning about behavioral changes in a system as it is redesigned, which extends beyond understanding how systems operate or react to stimuli. Findings from our past myosin GUI studies have suggested that it is difficult to relate how redesigning specific system components affects overall system behavior, even after solving multiple design problems where understanding of the problem space is gained (Egan et al., 2015b). These findings suggest that although knowledge of structures and behaviors are necessary for designing a system, there are additional skills or knowledge necessary in order to effectively design a system. These findings motivate our first hypothesis: *1) Knowledge of structures and behaviors in a system are not sufficient for human-based predictions of how a system's multi-level behaviors are altered during redesign.*

Development of a second hypothesis (assuming the first holds true) is now motivated by the need to discover what types of knowledge are teachable and improve human-based design of complex biological systems. Traditionally in medical domains, animations have proven successful in teaching students about complex functioning in physiological systems (Van Merriënboer and Sweller, 2010). A key consideration for effective teaching with animations is the reduction of cognitive load that impedes learning. An optimal cognitive load is achievable through chunking information and presenting them to a user through a series of small lessons, while also increasing the effort a participant exerts during learning that contributes to their understanding.

GUIs can also teach information beyond animations, through enabling human-interaction with virtual environments. Past cognitive studies have demonstrated that GUI environments where users are presented behaviors at two simultaneous system levels can improve their understanding of emergent system behaviors (Chi et al., 2012). These studies were conducted on diffusion systems that are built from two types of molecules, which are simpler models than multi-level muscle system models. Despite participants learning during the study, many participants were resistant to learning and fully understanding the emergent system behavior, which suggests that a single GUI approach for teaching muscles may impose too much complexity and cognitive load on a human learner. Therefore, an effective learning approach for multi-level biological domains could utilize a combination of animations and GUIs to teach how key structures and behaviors influence system functioning across levels. These considerations motivate our second hypothesis: 2) *Learning sessions bolstered with a multi-level design GUI will improve participants' capability for predicting altered behaviors across scales during redesign.*

A final consideration linked to successful design of complex biosystems suggests that designers should also reason about further effects of redesigning components of a system, since changes to one component in a complex system can influence the behaviors of components throughout the entire system. For instance, nanoscale alterations in muscles can influence disease states in the body as a whole (Moore et al., 2012). Therefore designers must also anticipate how synthetic muscle designs could influence the entire human body. The ability to predict causal chains of behavior throughout a complex system often grows with expertise, in part because experts tend to sort mechanisms by causal categories while novices sort information by domain-based knowledge (Rottman et al., 2012). Therefore, we predict: *3) Increased expertise leads to an increased capacity for predicting how the redesign of a complex system's subcomponents will influence system-wide functioning.*

These hypotheses are testable through a cognitive study that includes novices, experts, and GUI training interventions. Participants for this paper's study included differently trained experts to enable testing how varied amounts/types of knowledge and reasoning skills influence design. This was achieved through inclusion of mechanics experts represented by mechanical engineering doctoral students and physiology experts represented by medical students. The novice group consisted of STEM (science, technology, engineering, and mathematics) undergraduates, which were just beginning their careers in learning reasoning skills and knowledge that are essential for both engineering and medical disciplines. The choice of a multi-level muscle system ensured that it is familiar to all students at the macroscale, while likely being familiar only to physiology experts at the nanoscale. The aim of the cognitive study was to reach new insights concerning the knowledge, skills, and training necessary for effective human-centered design of complex multi-level biological systems, which could lead to many novel products for improved healthcare.

2 EXPERIMENTAL METHODOLOGY

The recruited participant groups included 12 STEM undergraduates that had completed no more than two years of undergraduate study in engineering, science and mathematics majors (novices), 11 mechanical engineering doctoral students that had completed at least one year of graduate studies (mechanics experts), and 10 medical students that had completed at least one year of medical school (physiology experts). All participants were recruited from two different universities in the Northeast United States. Each participant in the cognitive study was individually interviewed by the same interviewer using a standardized script. All sessions were recorded with an audio device that enabled post-experimental assessment of participant answers by two independent graders (a doctoral student in mechanical engineering with experience in myosin modeling and cognitive studies, and a senior undergraduate with chemical/biomedical engineering majors on a pre-med track) that formed a consensus on each measurement.

2.1 Cognitive Study Protocol

The cognitive study was divided into three primary phases, an initial phase for measuring prior participant domain knowledge, a second phase for assessing participating capabilities for predicting redesigned system behaviors for pre/post GUI support, and a final phase to determine participant capabilities in predicting system-wide effects when a subcomponent is redesigned.

The testing of participants' baseline knowledge is essential for determining that the medical student population is representative of physiological expertise, and that the muscle system is unfamiliar to other participant populations at the nanoscale. It was determined by asking the participant to describe the nanoscale proteins that power muscle contractions (to determine their knowledge of myosin and actin), and then the Figure 1 schematic was provided and further questions were asked (participants were allowed to keep this schematic throughout the entire study). Participants were asked to describe the interactions of components at the nanoscale (specifically the lowest level in Figure 1), and how this related to a complete muscle contraction. Upon completion of their descriptions, participants were notified that muscles work by having myosins attach to actin filaments while utilizing energy if they had not described those interactions; no further information was provided to participants. The reason for providing participants such knowledge is for testing the first hypothesis, which requires each participant to have knowledge of structures and behaviors in a system to determine if they aid in predicting effects on system behavior when redesigned.

The first hypothesis predicted that participants would perform poorly on redesign questions, and was tested through administration of such questions by showing participants a typical muscle and a muscle with an either increased or decreased cross-sectional area achieved by altering the number of fibers it contained. Increased and decreased muscle area questions were evenly distributed among participants, and the version of the question a participant received initially was different from later post-tests after GUI training sessions. Participants were asked to describe the effects on nanoscale and macroscale system behaviors, and measurements were collected to determine if participants could accurately predict the behavioral changes in muscle through structural and behavioral knowledge.

A training session for participants with animations and the multi-level GUI was the next protocol step, followed by a post-test of participants using the same muscle redesign question. During the animations training portion, participants were shown an animation of a fast contracting nanoscale filament system and a slow contracting system. They were told that the slowly contracting system utilized less energy and generated more force than the fast contracting system, and that each myosin always utilized one ATP per cycle. A print-out of the animation and provided information was given to each participant for the duration of the study to reduce the cognitive load required in their remembering these details. Participants were then guided through a learning session with the GUI that enabled users to alter myosin and muscle structures and receive output concerning force, velocity, and energy behaviors at both the nano and macroscale. After these sessions, participants were asked the same redesign question using for the muscle redesign condition they did not receive for their pre-testing questions. Comparison of pre/post-test results enables a comparison of whether the training sessions improved users' capabilities in predicting consequences on system behavior through redesign.

The last phase of the cognitive study seeks to determine whether expert participants are better able to predict outcomes of system-wide effects that emerge when lower level components of a system are redesigned, which is the focus of the final hypotheses. In this phase, participants were provided a schematic of a typical heart and an atypical heart with enlarged muscle tissue. They were asked to describe the effects that would result in a patient having the atypical heart in comparison to the typical heart, if everything else about the patient remained constant. The number of effects described by participants at higher levels are indicative of their ability to predict how redesign of system subcomponents affects entire system functioning.

2.2 Underlying Mathematical Multi-level Model of Muscle

The model in the GUI mathematically predicts nanoscale and macroscale outputs based on user inputs by averaging the behavior of myosins and determining their collective influences on macroscale functioning. At the nanoscale, the model is an extension of well-known biophysical models (Howard, 2001) that were used for design cases in past endeavors (Egan et al., 2013) to predict system behavior as myosin structures are altered. For this study's model, only lever arm length and myosin binding affinity design variables are controllable by a user, and have unique effects: 1) Lever arm length has a positive correlation with myosin size and filament velocity and 2) Binding affinity has a positive correlation with filament velocity and myosin energy consumption.

The model was extended to the macroscale by considering the contributions of all myosins in a muscle that is subject to an external force stimulus, and its physiological structure (Randall, 2001). Two muscle design inputs were included, the muscle area (through altering the number of in-parallel muscle fibers) and length (through altering the number of in-series sarcomeres). Changes to each design input have a unique effect: 1) An increase in muscle area is positively correlated with muscle velocity and energy use, and negatively correlated with individual myosin force output, although total force output of the muscle remains constant (since more myosins fit in a larger muscle, but the macroscopic stimuli is the same). 2) An increase in muscle length has a constant macroscopic force, a positive correlation with muscle velocity (since there are more sarcomeres in series), a positive correlation with muscle energy (since there are more total myosins) and constant behavior for myosins (since all additional in-series units added to the muscle result in no net change in muscle force or how force is distributed among myosins).

Prediction of design effects is often non-obvious and requires careful consideration of which design input is being altered, and makes redesign problems challenging for humans to solve. These considerations make redesign problems insightful within the cognitive study since they are not easily solvable, but are still informed by domain knowledge relevant to the design space. Additionally, redesign scenarios are prototypical in bio-based design, since engineers typically leverage known biological structures and reconfigure them for artificial purposes.

2.3 Multi-level Graphical User Interface

The mathematical model was embedded in a GUI such that design inputs are manipulated via slider bars and behavioral outputs are plotted. When introducing the GUI to participants, they are told that all myosins in a muscle are always identical, therefore altering the nanoscale structure of a myosin results in all myosins within the muscle changing. Renderings of a single muscle and myosin in the GUI (Fig. 2) update in real-time to reflect design changes—the muscle schematic's height and width change in size, while the myosin schematic's height and the arrow next to it (which represents binding affinity changes) change in size to reflect differences in relevant design inputs.

The resulting system behavior at the nano and macroscales was output visually across plots that represent the 8 unique pair-wise combinations of 4 design inputs as independent variables (muscle area, muscle length, myosin lever arm length, and myosin binding affinity), and 2 behavioral outputs (nano/macro velocity and energy usage). The third output behavior, force, is communicated via text because it is assumed constant at the muscle scale, and only changes for myosins when lever arm length changes. Additionally, the muscle contraction force (which is constant) and time average force per myosin is presented via text to convey these spatial relationships to users. The GUI was developed with Java using the JavaFX 2.0+ API and is presented in Figure 2.

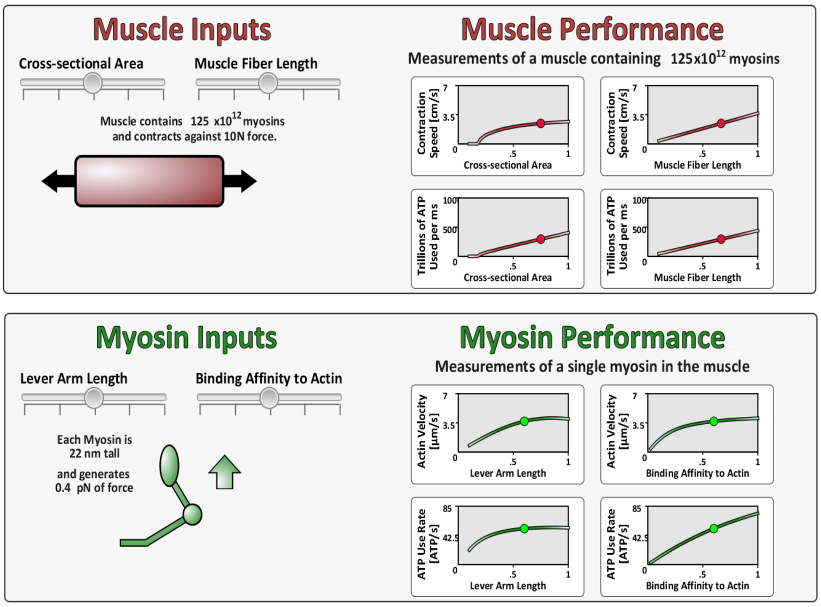


Figure 2. Multi-level GUI for designing muscles and myosins

The goal of the GUI is to train users in critical domain-based and multi-level reasoning concerning the system, through demonstrating how design alterations of one parameter affect the behavior of the system at both scales. To reduce cognitive load and promote learning, modules are added in steps during GUI training sessions. First, the GUI is presented with only the design inputs and schematics of myosin and muscle, text stating the force and size of the muscle, and the size of each myosin. Users are then asked how they expect a change in each design slider to affect the number of myosins in the system, which is increased by increasing muscle area or muscle length, decreased by increasing lever arm length, and not affected by binding affinity. Upon answering each question, the interviewer then changes the slider to show the user whether they were correct or not and then provides the proper explanation if necessary. Through this strategy, learning is improved through having participants put forth effort into their reasoning processes, which optimizes cognitive load that facilitates learning. After the exercise is completed for each slider, it is repeated through adding the myosin force text to the GUI and asking the same set of questions. After this round is completed, one more round is conducted by asking how each design parameter will affect the velocity of the muscle or myosin as relevant charts are included. Through these exercises, a user is expected to learn the effects of changing a design input on both the nano and macroscales, and inter-level relationships such as how the number of myosins is altered through lever arm and muscle design changes.

3 COGNITIVE STUDY RESULTS

The results for the cognitive study are presented in three sections that reflect the three phases of the study protocol: First, a baseline measurement for determining prior knowledge and familiarity of muscle structures and behaviors is presented, then pre/post-training results to determine the effectives of a GUI-based training session, and lastly an assessment of how well each group could predict the multi-level effects of a redesigned system.

3.1 Baseline Measurement for structures and behaviors

A baseline measurement was conducted to determine the knowledge each participant had with multi-level muscle structures and behaviors prior to any learning interventions. Participants were asked to describe how muscles work at the lowest level illustrated in Figure 1, and how the lowest level behaviors influenced muscle contraction as a whole. A key was created by two independent graders listening to all interview session recordings and identifying components mentioned in the following categories: nanoscale structures, nanoscale behaviors, inter-level behaviors. Any structure or behavior that was mentioned by at least two participants was added to the key, which filtered out obscure structures and behaviors to create a relevant grading scheme for comparison across groups.

The nano-level structures of the key consisted of: myosin, actin, ATP, calcium, and tropomyosin, with calcium and tropomyosin being nanoscale molecules that regulate when myosins can begin utilizing ATP and attaching to actin. Three nano-level behaviors were included in the key: myosin binding to actin (attachment), myosin force exertion on actin (power-stroke), and ATP being decomposed into ADP as its energy is transduced by the myosin (detachment). These three nano-level behaviors correspond to the three primary behaviors of myosins that are crucial to understanding the myosin design space (Egan et al., 2013). Inter-level behaviors included the sliding of filaments at the nanoscale enabling sarcomere contraction, and the contraction of sarcomeres enabling muscle contraction, which represent cases where higher level contraction emerges from non-contracting myosin behavior and when higher level contraction emerges from lower-level contraction of sarcomere units. Using this key, each participant was provided a score of 1 or 0 depending on whether they correctly cited and described a structure or behavior, and results were aggregated for each group and presented in Figure 3.

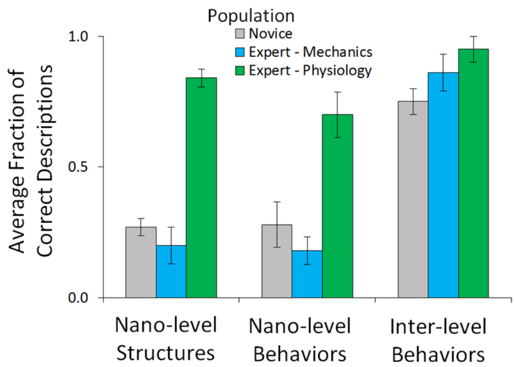


Figure 3. Structures and behaviors known by each participant group

The results demonstrate that the physiology expert population possessed greater domain knowledge of nano-level structures than the novice ($p < 0.001$) and mechanics expert ($p < 0.001$) populations and greater domain knowledge of nano-level behaviors than the novice ($p < 0.002$) and mechanics expert ($p < 0.001$) populations. There were no significant differences between the novice and mechanics expert populations for these metrics. This data reinforces the notion that medical students are representative of an expert population with different knowledge than engineers, and could potentially utilize information beyond what is presented to populations within this study to solve questions. Additionally, it suggests that the physiology expert population is more familiar with the concepts that were taught to all participants; however, this familiarity could introduce challenges if their previous training is in conflict with concepts presented in this study (as found in the next phase).

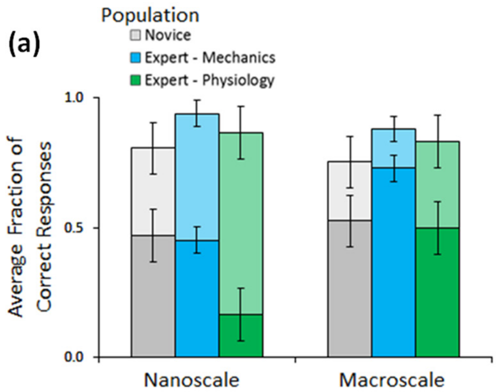
All groups had a high rate of describing inter-level behaviors, with no statistically significant differences, which suggests that it is quite plausible for even novices to understand how muscles work across scales. Such mechanical insights could have been reached by non-expert populations by inferences from the provided schematic and knowing that macroscopic muscles contract.

Before continuing to the next phase of the experiment, the interviewer provided information that myosins attach to filaments, exert force, and then detach and utilize energy to participants that did not demonstrate such understanding. By ensuring all participants have the same basic knowledge of key structures and behaviors, the next phase of the experiment can assess whether that knowledge aids in reasoning about alterations in system behaviors as it is redesigned.

3.2 Multi-level design reasoning

Participants were given redesign questions and asked to describe at the nanoscale and macroscale whether force, velocity, and energy consumption increased, decreased, or remained the same after system redesign. These questions were asked pre/post-training and the number of correct responses aggregated for each group are presented in Figure 4 with regards to pre/post-training correctness of responses at each scale (Fig. 4a; darkly shaded areas represent pre-training responses, while lightly shaded areas represent post-training responses) and each effect pre/post-training (Figs. 4b and 4c).

(a)



(b)

% Correct Responses Pre-GUI Training	Nanoscale			Macroscale		
	Force	Velocity	Energy	Force	Velocity	Energy
Novice	0.5	0.58	0.33	0.58	0.58	0.42
Expert-Mech	0.82	0.36	0.18	0.73	0.64	0.82
Expert-Phys	0.2	0.2	0.1	0.5	0.5	0.5

(c)

% Correct Responses Post-GUI Training	Nanoscale			Macroscale		
	Force	Velocity	Energy	Force	Velocity	Energy
Novice	0.92	0.75	0.75	0.67	0.92	0.67
Expert-Mech	1	0.91	0.91	0.82	1	0.82
Expert-Phys	1	0.9	0.7	0.8	1	0.7

Figure 4. Percentage of correct response pre/post GUI via plots and tabulations.

The first hypothesis proposed that *Knowledge of structures and behaviors in a system are not sufficient for human-based predictions of how a system's multi-level behaviors are altered during redesign*, which is supported by no groups having greater than 50% correctness on nanoscale redesign questions pre-training. Further, physiology experts that had the most prior domain knowledge correctly answered less than 17% of the redesign effects at the nanoscale, which is significantly different from the novice ($p < 0.007$) and mechanics expert ($p < 0.014$) groups. The second hypotheses stated that *Learning sessions bolstered with a multi-level design GUI will improve participants' capability for predicting altered behaviors across scales during redesign,* which is supported by all groups showing improvements for all questions post-training in comparison to pre-training correctness with statistical significance of ($p < 0.008$), with the exception of mechanics experts performing well on macroscale questions both pre/post testing.

Going beyond the tested hypotheses, Figure 4a shows that mechanics experts performed better than other groups as a whole ($p < 0.044$) when considering macroscale phenomenon. This suggests that their training is well-suited for mechanically-based problems at macroscales, which is a cornerstone of engineering education. Physiology experts performed worse on nanoscale reasoning than other groups, which suggests that their past training may have biased them towards thinking about relationships in the design space ineffectively for solving mechanically-based redesign problems. In Figure 4b, mechanics experts performed significantly better than physiology experts ($p < 0.003$) for correctly assessing the force at the nanoscale, which suggests their expertise is important for biological design domains in addition to physiological knowledge. These measurements demonstrate that despite the differences in initial knowledge and problem solving skills by each participant group, that GUI-based training aid in promoting effective reasoning within and across scales.

3.3 Reasoning about Patient Health

The final hypothesis proposed that *Increased expertise leads to an increased capacity for predicting how the redesign of a complex system's subcomponents will influence system-wide functioning.* Participants were presented schematics of a typical distribution of heart muscle tissue and an atypical distribution that is enlarged for certain areas of the heart (Figure 5). Dark red areas in the schematic highlight the differences in muscle tissue distribution for the two hearts. Participants were asked to describe the effects that having an enlarged heart may have on a patient. The number of effects participants described at four different levels of scale: Molecular scale effects (e.g. myosin generates more force), tissue effects (e.g. muscle contracts faster), organ effects (e.g. heart has larger volume), and bodily effects (e.g. patient has possible dizziness) were counted. The results are presented in Figure 5 for the average number of effects described at each scale.

The results show that all groups described a similar number of effects at the molecular and tissue scales (no statistically significant differences were found). The finding supports the notion that the design GUI was effective in teaching myosin and muscle related phenomenon, as the physiology expert population did not bring in outside information to describe effects beyond those of the GUI.

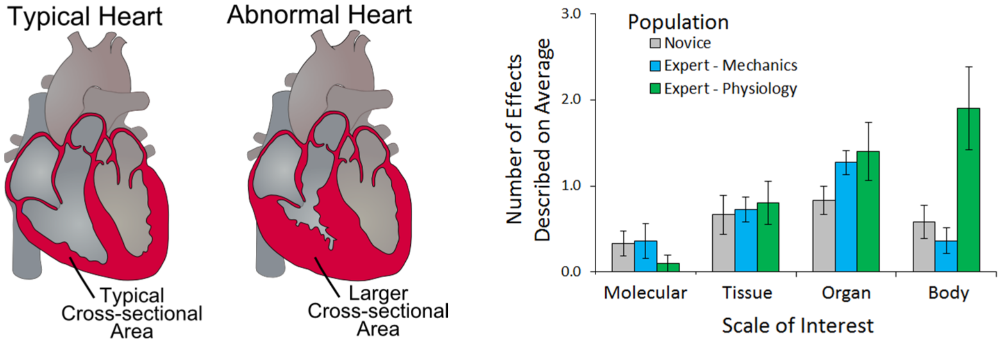


Figure 5. Heart schematics and number of effects describe across scales by participants.

At the organ scale, mechanics and physiology experts as a whole described an increased number effects in comparison to the novice group ($p < 0.47$). This findings suggests that in addition to supplementary domain knowledge that physiology experts may possess, these groups may benefit through expertise in knowing how to reason about complex systems generally, rather than domain specific manners novices tend to utilize (Rottman et al., 2012). Through having a generalized organization of knowledge about the system, these experts are suggested to better predict effects beyond the domain knowledge taught from the GUI sessions, whereas novices focused on the molecular and tissue scales where domain knowledge was taught explicitly by the GUI. Additionally, they may be better skilled at intuiting effects from analyzing the schematic itself, such as the visibly smaller chamber in the atypical heart leading to increased blood pressure in that region.

Physiology experts outperformed both the novices ($p < 0.026$) and mechanics experts ($p < 0.011$) in describing bodily level effects, which can be explained through their previous training as medical students and familiarity with cardiac hypertrophy diseases (Moore et al., 2012). They may additionally have better schemas for organizing system interactions and generalizing effects pertinent to health based on their expertise in human physiology.

These findings support the hypothesis that expertise leads to improved reasoning about system-wide effects through structural alterations representative of redesign problems, which is a necessary skill when considering any biological design utilized in health care will have potential interactions with the entirety of a patient's bodily systems.

4 DISCUSSION AND CONCLUSION

Emerging bio-based design applications, such as organ printing, are creating blurs among engineering and medical fields. One of the greatest challenges in creating products is the traversal of non-obvious multi-level relationships within bio-based design spaces. In this study, a multi-level mathematical model and design GUI were created for testing the understanding, learning, and reasoning processes of novice (STEM undergraduates), mechanics expert (engineering doctoral students), and physiology expert (medical students) populations for multi-level muscle systems. A cognitive study was conducted that measured participant's initial knowledge, pre/post-training capabilities for assessing behavioral changes at different scales when the system is redesigned, and whether they could relate subsystem alterations to effects to system-wide functioning.

Three hypotheses were tested, which were all supported by empirical measurements. The first hypothesis proposed that *Knowledge of structures and behaviors in a system are not sufficient for human-based predictions of how a system's multi-level behaviors are altered during redesign*. It was supported by all groups performing poorly on initial muscle redesign questions, including physiology experts that possessed a high amount of structural and behavioral knowledge of muscles prior to the study. The second hypotheses stated that *Learning sessions bolstered with a multi-level design GUI will improve participants' capability for predicting altered behaviors across scales during redesign.* It was supported by all groups showing significant improvement on multi-level redesign questions when comparing pre/post-training performance. The final hypotheses proposed that *Increased expertise leads to an increased capacity for predicting how the redesign of a complex* *system's subcomponents will influence higher level system functioning.* It was supported by physiology experts describing more whole body effects that could emerge from an enlarged heart muscle, and both expert groups describing more organ level effects in comparison to novices.

These findings suggest that knowledge of the structures, behaviors, and functions of a system, which is widely regarded as beneficial for understanding and communicating changes in complex systems, are not sufficient for redesigning complex multi-level biological systems. Participants were shown to properly understand redesign influences in the design space once they completed learning sessions with a multi-level GUI, and learning successes by the novice group demonstrated that the learning sessions were highly effective, even for non-experts. Mechanics and physiology experts also had contrasting skill sets—mechanics experts had greater intuition for describing force distributions, while physiology experts could better extrapolate how alterations in muscle affect patient health. These findings lay the foundation for studying bio-based design intersections across medicine and engineering, which has great potential in promoting healthier lives.

REFERENCES

CHI, M., ROSCOE, R., SLOTTA, J., ROY, M. & CHASE, C. 2012. Misconceived causal explanations for emergent processes. *Cognitive Science,* 36, 1-61.

EGAN, P., CAGAN, J., SCHUNN, C. & LEDUC, P. 2013. Design of complex biologically based nanoscale systems using multi-agent simulations and structure-behavior-function representations. *Journal of Mechanical Design,* 135, 061005.

EGAN, P., CAGAN, J., SCHUNN, C. & LEDUC, P. 2015a. Improving understanding and design proficiency of complex multi-level biosystems through animation and parametric relationships support. *submitted*.

EGAN, P., CAGAN, J., SCHUNN, C. & LEDUC, P. 2015b. Synergistic human-agent methods for deriving effective search strategies: the case of nanoscale design. *submitted*.

GIANNATSIS, J. & DEDOUSSIS, V. 2009. Additive fabrication technologies applied to medicine and health care: a review. *The International Journal of Advanced Manufacturing Technology,* 40, 116-127.

HAMBURG, M. A. & COLLINS, F. S. 2010. The path to personalized medicine. *New England Journal of Medicine,* 363, 301-304.

HMELO-SILVER, C. E., MARATHE, S. & LIU, L. 2007. Fish swim, rocks sit, and lungs breathe: Expert-novice understanding of complex systems. *Journal of the Learning Sciences,* 16, 307-331.

HOWARD, J. 2001. *Mechanics of Motor Proteins and the Cytoskeleton* Sunderland, MA, Sinauer Associates, Inc.

JORDAN, R., HMELO-SILVER, C., LIU, L. & GRAY, S. 2013. Fostering Reasoning About Complex Systems: Using the Aquarium to Teach Systems Thinking. *Applied Environmental Education & Communication,* 12, 55-64.

KORIN, N., KANAPATHIPILLAI, M., MATTHEWS, B. D., CRESCENTE, M., BRILL, A., MAMMOTO, T., GHOSH, K., JUREK, S., BENCHERIF, S. A. & BHATTA, D. 2012. Shear-activated nanotherapeutics for drug targeting to obstructed blood vessels. *Science,* 337, 738-742.

MOORE, J. R., LEINWAND, L. & WARSHAW, D. M. 2012. Understanding cardiomyopathy phenotypes based on the functional impact of mutations in the myosin motor. *Circulation Research,* 111, 375-385.

RANDALL, D., W. BURGGREN, AND K. FRENCH 2001. *Eckert Animal Physiology: Mechanisims and Adaptations* New York, W.H. Freeman and Company.

ROTTMAN, B. M., GENTNER, D. & GOLDWATER, M. B. 2012. Causal systems categories: Differences in novice and expert categorization of causal phenomena. *Cognitive science,* 36, 919-932.

VAN MERRIËNBOER, J. J. & SWELLER, J. 2010. Cognitive load theory in health professional education: design principles and strategies. *Medical education,* 44, 85-93.

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