Adv Physiol Educ 45: 880–885, 2021.
First published September 2, 2021; doi:10.1152/advan.00108.2021

american physiological society

ADVANCES IN PHYSIOLOGY EDUCATION

A PERSONAL VIEW

What do we mean when we talk about "structure/function" relationships?

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Abstract

In multiple studies "structure/function" has been identified as an important core concept in biology and physiology. Teachers expect their students to be able to use this concept in making sense of physiology. However, it is unclear exactly what physiologists are referring to when they use the term "structure/function." Here I first offer examples of four different ways in which I have used the term in the classroom. Then, I propose a conceptual framework that is an explicit statement of the "structure/function" core concept that can be used by teachers and their students as they attempt to master physiology. Determining whether this conceptual framework is completely accurate and whether it will prove useful in the classroom will require feedback from physiology teachers who attempt to use it in their classroom with their students.

core concepts; conceptual frameworks; structure/function

INTRODUCTION

In 2009, the American Association of Medical Colleges (1) published a report outlining the appropriate preparation in the sciences needed for future physicians; it focused on a set of core concepts and competencies. That same year the American Association for the Advancement of Science hosted a meeting to examine the state of biology education in the United States and in 2011 issued its final report (2). Here too, one focus was on identifying the core concepts of biology. Also, in 2009 Michael et al. (3) attempted to identify a set of core concepts for physiology. In 2011 Michael and McFarland (4) surveyed physiology teachers to determine what they viewed as the core concepts, and in 2020 they revisited the core concepts that had been identified by faculty (5).

Finally, in 2020 Stanescu et al. (6) surveyed undergraduate physiology programs to determine faculty and student attitudes about the core concepts of physiology. At the same time Crosswhite et al. (7) surveyed a different group of faculty members about their use of core concepts of physiology.

In all of these reports, "structure/function" was identified as one of the core concepts of physiology that students ought to understand and be able to use.

Given the widespread acknowledgment that "structure/function" is an important core concept of physiology it is fair to ask what exactly this core concept means and how, in fact, this concept is to be used in the teaching and learning of physiology. In this paper I will *1*) discuss the lack of definitions for the terms making up "structure/function," *2*) describe how I have used this concept in the classroom, and *3*) propose a conceptual framework for "structure/function."

WHAT DOES "STRUCTURE/FUNCTION" MEAN?

The reports establishing the importance of the core concept of "structure/function do not in fact define the meaning of "structure/function" in any useful way. Yoho et al (8) carefully examined the use of these terms across many different STEM disciplines (plant biology and ecology**, anatomy and physiology** {emphasis added}, chemistry, mathematics and statistics, engineering, and physics) and observed "... we found a glaring lack of definitions for the meaning of *structure and function* as a phrase representing the educational concept or as individual terms, *structure and function*. From our observations across multiple disciplines and professional societies, we speculate that there may be additional ambiguity in the meaning of the phrase *structure and function* as a whole as well as the individual contributing terms, *structure and function*, especially among STEM disciplines."

Perhaps one possible consequence of the lack of clearly defined terminology is that student understanding of this core concept is weak. Carter and Prevost (9) studied physiology students' ability to define "structure/function relationships" and to provide examples under two different testing protocols. Even under the most successful of the protocols, fewer than half of the students were successful at the assigned tasks; student performance in the other protocol was significantly poorer. Stanescu et al. (6) surveyed physiology faculty and students about structure/function relationships and found that faculty rated this core concept as highly important. Students too thought it was important, but also thought it unlikely that they would remember this core concept in five years.

It is thus fair to ask what we, physiology teachers, mean when we talk about structure and function and use the

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Submitted 15 July 2021 / Revised 31 August 2021 / Accepted 31 August 2021

expression "structure/function" relationships in attempting to help our students gain an understanding of physiology.

One dictionary definition (biologyonline.com) of structure is "(*biology*) An arrangement or organization of parts to form an organ, system, or living thing." "Structure" then refers to the arrangement of the components making up a physical entity, whether that be a molecule, a cell membrane, cell, tissue, or organ. At each organizational level in the body, structures are describable by different characteristics: area, thickness, macroscopic form or shape, microscopic arrangement of the parts, sequence of amino acids, etc.

"Function" is defined (biologyonline.com) as "(*biology*) The special, normal, proper physiologic activity of a body part or an organ." However, physiologists distinguish between "function," which is what the entity does and why it does it, and "mechanism," which is a description of how the entity carries out that function (10).

The core concept of "structure/function" is thus used to convey the idea that there is always a relationship between the structure of a biological entity and the functions (and sometimes the mechanisms) carried out by that entity.

What did the physiologists who participated in the Michael and McFarland survey (4) mean when they cited "structure/function" as a core concept?

An examination of the written responses seen in Table 1 makes clear that there can be a lack of specificity present when physiology teachers invoke "structure/function" as an important concept for their students to understand. While these comments were made 10 yr ago, and faculty familiarity with the core concepts has changed in the intervening years (6, 7), they still seem representative of what our colleagues mean by "structure/function."

Can physiology textbooks help us define what is meant by "structure/function?" Three popular textbooks used in courses at three different levels were examined to try to answer two questions: do these books identify "structure/function" relationships as a core concept (or some related term), and do they then use the core concept in their descriptions of relevant physiological phenomena? The books examined were Saladin's (11) anatomy and physiology book used in undergraduate courses, Silverthorn's book (10), which is used in undergraduate physiology courses, and Koeppen and Stanton (12), which is aimed at medical students.

The full title of Saladin's book (11), *Anatomy & Physiology: The Unity of Form and Function*, certainly implies a focus on the relationship between structure (form) and function. In the first chapter (section 1.8) the author defines six major "themes" (core concepts) and lists "the unity of form and function" as one of them. It is worth noting that each of the six major themes defined here is also listed in Michael and McFarland (4, 5) as a core concept.

Silverthorn (10) also describes five "themes" including "structure and function across all levels of organization." Here too, all the themes described are all represented in Michael and McFarland's list of core concepts (4, 5).

However, neither Saladin nor Silverthorn use the theme (or core concept) of "structure/function" relationships in discussions about those phenomena to which it is most obviously applicable (see below).

Koeppen and Stanton (12) use the term "structure and function" only once to refer to an overview of the respiratory system in which both anatomy and physiology are presented, but they do not define this as a recurring theme or core concept.

While the examples cited are a very small sample of all available physiology textbooks, it would appear that textbook authors are no more specific about what "structure/function" means as a core concept (or theme) than were the respondents to the Michael and McFarland survey (4).

The fact that it seems so difficult to identify what "structure/function" means and how students are to use it, does not mean that this core concept is unimportant. It does mean that the physiology teaching community will need to work to reach a consensus on this question. If we cannot clearly communicate about what we mean, students will not be able to employ this concept in their attempt to understand physiology.

THE "STRUCTURE/FUNCTION" CORE CONCEPT

Three published descriptions of the "structure/function" core concept (1, 2, 8) can be found in Table 2.

The similarities between these three statements are obvious, but each of them suffers from the same lack of any explicit reference to how this concept is to be applied in thinking about physiological mechanisms. As such, the term "structure/function" (see Tables 1 and 2) is simply a truism; we must always understand the structure generating a function in order to fully understand that function. For example, to fully understand the pumping action of the heart (function) you must understand the anatomy of the heart (structure).

Table 1. *Definitions of "structure/function" by faculty*

Definitions
Examples of nonspecific reference (no examples of application described) to "structure/function" relationships (total of 19)
(1) "Structure (histology and anatomy) can inform about physiological function because structure and function are inter-related."
(2) "Structure/function relationships. Structure determines function and if the structure is altered, the function is altered."
(3) "Macro compared to micro structure underpinning function"
(4) "Changes in shape result in a change in function."
(5) "Form and function are related-form determines function."
Specific reference to actual applications of "structure/function" core concept (total of 2)
(6) "Protein structure and the implications of changes in structure for function and dysfunction."
(7) "Repeating structure/function motifs, like elaboration of surface area to volume ratios, counter-current multiplication/exchange mechanisms, etc."

See Ref. 4.

Table 2. *The core concept of “structure/function”*

Core Concept
From *Vision and Change Report* (Ref. 2; focused on biology education)
“2. STRUCTURE AND FUNCTION: Basic units of structure define the function of all living things.”
From *Scientific Foundations for Future Physicians* (Ref. 1; focused on pre-med education)
“Competency E5: Demonstrate knowledge of how biomolecules contribute to the structure and function of cells.”
“Competency E6: Apply understanding of principles of how molecular and cell assemblies, organs, and organisms develop structure and carry out function.”
From Michael and McFarland (Ref. 5; focused on physiology education): note that Michael and McFarland have used the linking symbol ↔ to signal the fact that the interaction between the structure and function runs in both directions.
“The functions of molecules, cells, tissues, or organs are determined by their form (structure). Structure and function (from the molecular level to the organ system level) are intrinsically related to each other.”

WHAT DO I MEAN WHEN I USE THE “STRUCTURE/FUNCTION” CORE CONCEPT?

The “structure/function” core concept is one of five core concepts that Michael and McFarland (5) have described as being “ways of looking at the world.” They serve as thinking tools used by physiologists when they confront any problem or question about a living organism. These concepts often represent a kind of tacit (or implicit) knowledge (5); “knowledge that usually is not openly expressed or taught” but is used in practice (13). This seems an apt description for “structure/function” for most physiology teachers.

I have used the “structure/function” core concept in at least five different ways in helping students make sense of physiology. The physiology textbooks referred to above (10–12) contain descriptions of most of the phenomena I discuss below.

Like the textbook authors cited above, I have used the phrase “structure/function” in the classroom simply to refer to the fact that to understand the function of a system you must understand structure of that system. It is a signal to the students that both the anatomy (structure) and the physiology (function) will be considered as they seek to understand physiology. This is the usual admonition used by physiology teachers and physiology textbook authors. Whether this core concept is of any use to students when left as an admonition is open to question.

However, I have also used “structure/function” concept in four quite specific ways to assist students in their attempt to master physiology.

First, I have used “structure/function” to emphasize the importance of understanding the arrangement of the system components (structure or anatomy) that gives rise to a mechanism or response (function or physiology).

The heart offers several examples of “structure/function” relationships that are important for students to understand. Conduction of the excitation generated at the sinoatrial node spreads across the atria by cell-cell communication; cardiac muscle cells, unlike skeletal muscle cells, have gap junctions between myocytes through which current generated by one cell can stimulate neighboring cells. Excitation reaches the atrioventricular node where it is delayed, thus ensuring that the atria can fill the ventricles before the ventricles contract. The spread of excitation through the ventricles is facilitated by the presences of the Purkinje fibers making possible the coordinated contraction of the ventricular myocardium in an orderly way that allows the heart to pump blood. Function, the pumping of blood, is dependent on the characteristics of the structures that do this work.

Consider the fact that the heart is two pumps in series; the right heart right perfuses the lungs while the left heart perfuses the rest of the body. The flow of blood through the heart, and the filling of the ventricles, is determined by the presence of four heart valves. The opening and closing of these valves are determined by their location and the pressures that are present on either side of the valves. When the valves fail to open and close properly, cardiac function is altered.

One final example is particularly illustrative of the importance of thinking about the structure and the function of a physiological system. Rall (14) has described the research undertaken to understand the final mechanism linking skeletal muscle excitation and the contraction of the excited muscle. Advances on two fronts, one morphological (structure) and the other physiological (function), were required to solve this problem. Thus, students need to understand both the structure of the T-tubules and the function of the gated channels in the membrane in order to understand excitation-contraction coupling.

Second, I have also used “structure/function” to signal to my students the importance of the dimensions (surface area and thickness) of a structure vis-a-vis passive transport processes between compartments in the body. This use of the term “structure/function” is alluded to in *response 7* in Table 1. There are, of course, a great many examples of this that are important topics in all physiology courses.

Solute movement (flux) across any membrane is described by the Fick equation which contains two structural quantities that contribute to determining the flux. One common representation of this equation is:

$$J = -\mathrm{D}A(\Delta \mathrm{C}/\Delta X),$$

where D is the diffusion coefficient, A is the area over which diffusion can occur and X is the distance between the two compartments being considered (the thickness of the barrier). What this tells us is that the larger the area over which diffusion can occur, the greater the flux for any concentration gradient. On the other hand, the greater the distance over which diffusion must occur the smaller the flux. This fundamental physical relationship (a relationship between structure and function) can then be applied to a number of other phenomena.

For example, the movement of oxygen and carbon dioxide in the lungs and in the tissues must meet the metabolic needs of the body. Both gases move by passive diffusion, and a physiologically adequate flux of each gas is dependent on there being a large surface area across which diffusion down a concentration gradient can occur. The structure of the alveolar space provides the large area for oxygen uptake and carbon dioxide elimination, and the very small diffusion distance presents further enhances the gas exchange.

In the tissues, gas exchange between capillary beds and the perfused tissue is facilitated by the thin walls of the capillaries, and the high density of capillaries ensures a large surface area. In addition, the distance gases must move between the capillaries and the cells is small.

Consider a very different phenomenon, the active absorption of carbohydrates and proteins in the small intestine. This process is facilitated by an essential structural adaptation, the presence of villi and microvilli, which dramatically increases the surface area of the mucosal surface of the small intestine. This in turn allows for an increase in the number of membrane transporters through which absorption can occur.

Third, "structure/function" also refers to an essential property of the many protein molecules that play important roles in essentially every physiological process. This was explicitly alluded to in *response 6* seen in Table 1.

The three-dimensional structure of protein molecules is determined, in part, by the physicochemical environment in which they are present. This results in a large number of important physiological phenomena (many of the following examples are discussed in Ref. 12).

Enzymes, which are proteins, are inactivated or activated when certain ions bind to them. Changes in pH, or phosphorylation-dephosphorylation, change the structure of enzymes and hence change their activity.

Ligand binding to cell membrane receptors (proteins) can give rise to a cascade of molecular changes in which the structure of protein molecules is altered to either increase or decrease their activity.

When the three-dimensional structure of membrane channels, whether ligand-binding or voltage-gated, is altered, the passage of certain ions through the water filled pore is enabled. Channel selectivity (which ions can pass through the pore) is itself is a function of the structure of the channel protein, and changes in structure of these proteins will alter their function.

A final example: when a hemoglobin molecule binds the first oxygen molecule the structure of the hemoglobin molecule is changed, causing its affinity for additional oxygen molecules to change. Binding of carbon dioxide or hydrogen ions to hemoglobin changes its structure, changing the binding of oxygen.

Fourth and finally, Michael and McFarland (8) recognized that the relationship between structure and function runs in both directions and suggested that "structure ↔ function" would better serve to remind students that changes in function or use can give rise to changes in structure.

For example, long-term exercise (a change in function) results in hypertrophy of the exercising muscle (a change in structure). Exercise can also lead to conversion between the two types of fast-twitch fibers. Of course, lack of use of a muscle (a change in function) can lead to atrophy of the muscle (a change in structure).

Weight-bearing exercises (function) alter bone remodeling and can lead to changes in the shape (structure) of the affected bones. Extended periods of time under zero gravity conditions (a change in function) lead to decalcification of bone and changes in bone density (a change in structure).

One final example is the effect of aerobic exercise training; the heart has to work harder, leading to a number of changes to the cardiac vasculature that improve cardiac performance.

It should be noted that while the three physiology textbooks discussed above (10–12) do not explicitly refer to the "structure/function" core concept, they all discuss the many examples of how this core concept can be used to help students make sense of physiology.

WHAT MIGHT A CONCEPTUAL FRAMEWORK FOR "STRUCTURE/FUNCTION" LOOK LIKE?

My colleagues and I (15) have argued that when students understand a core concept, can recognize where it is applicable, and can successfully apply the concept to making sense of a physiological phenomenon, this facilitates their mastery of physiology. We also argued that one key to helping students use core concepts is to explicitly invoke them whenever they are applicable to the physiology topic at hand.

To do this we need a clear sense of what the core concept encompasses. The process of "unpacking" the core concepts is thus a necessary starting point (15). This was, in part, one of our motives for "unpacking" four of the core concepts, "flow down gradients" (4), "homeostasis" (16), "cell-cell communication" (17), and "cell membrane" (18), creating and validating conceptual frameworks for each of them. These frameworks can be used by the teacher to determine how and when to use a particular concept and by students as a scaffolding for applying the concept to the topic at hand. Furthermore, the framework for the "homeostasis" core concept (16) served as the starting point for the development and validation of a concept inventory to assess student understanding of this concept (19).

However, when we consider the core concept of "structure/function" what has been lacking is an explicit formulation of what physiologists mean by this concept. Above, I have described four different ways in which this core concept has been incorporated into my teaching about physiological phenomena. It might be helpful to physiology teachers to have a conceptual framework that explicitly defines how we use this core concept.

Can a conceptual framework for "structure/function" be created? If so, what would it look like? Finally, how could it be used by instructors or students?

All of the conceptual frameworks that we have created and validated (4, 16–18) are hierarchically organized descriptions of the smaller ideas that make up the core concept. They vary in size (number of statements) and complexity (number of levels in the hierarchy). Each was validated by asking respondents to rate the importance of their students understanding each of the statements making up the framework.

However, as I suggested above, "structure/function" is a kind of admonition, a reminder to students, that physiological functions at every level of organization arise out of some structure and that understanding the function requires understanding the structure. This reminder can be used to illuminate a number of physiological phenomena, but the list of examples I presented here is far smaller than the instances when it is clearly relevant. Table 3 contains a proposed (but not validated) conceptual framework that describes the ideas that make up the core concept of "structure/function" as I have used it (see above).

This conceptual framework differs from the frameworks for flow down gradients (4), homeostasis (16), cell-cell communications (17), and cell membrane (18), in that it merely attempts to explicitly expand the definition of "structure/function" that Michael and McFarland provided (5) based on my experience as a physiology teacher. In this regard it is similar to the conceptual framework for "mass balance" (20).

There are two obvious questions about this proposed conceptual framework. Is it accurate? That is, does it capture the various ways in which the core concept of "structure/function" is used by physiology teachers? In addition, is it of any use to physiology teachers and their students?

To the extent that teachers expect their students to be able to apply the core concept of "structure/function" to facilitate their mastery of physiology, the conceptual framework may prove helpful. Ultimately, the utility of this core concept for students will depend on pedagogical decisions made by the teacher.

CONCLUSIONS

Physiology educators and teachers believe that the core concept of "structure/function" is an important one, and it is one that they ask their students to use in attempting to make sense of physiology. However, for students to be successful it is essential that instructors provide explicit descriptions of what they mean by that expression in the context of whatever the current physiology topic might be.

I have proposed that the "structure/function" core concept refers to four different ways in which structure and function relate to one another in thinking about different physiological phenomena. The conceptual framework I have presented here, while not yet validated, will hopefully serve as the starting point for a discussion about this important core concept means.

It is my hope that publishing my thoughts about a conceptual framework for "structure/function" will contribute to the physiology teaching community working towards a consensus about what this core concept means. The next steps would be to create a consensus conceptual framework and then validate it as was done with the core concepts of "flow down gradients" (4), "homeostasis" (16), "cell-cell communications" (17), "cell membrane" (18), and "mass balance" (20). Once a "structure/function" conceptual framework has been generated the work of producing a concept inventory can proceed (19).

Michael et al. (15) have suggested that one key to helping students use the core concepts as learning tools is the explicit, consistent, and repeated use of them where they are applicable. Merely referencing the term "structure/function" would not be enough. Specific reference is needed about how it is to be used in the context of the moment. The conceptual framework I have proposed here is a first attempt to meet this need, but I have no doubt that others will be able to point to additional ways in which "structure/function" is used.

Whether this framework is a useful one for teachers and students will only be determined as it, or alternatives, are used in more physiology courses and physiology programs than those surveyed by Stanescu et al. (6) and Crosswhite et al. (7). In this context, it should also be noted that not every core concept will be used in every course or curriculum. The choice of whether to emphasize the core concept of

Table 3. *A proposed conceptual framework for the core concept of "structure/function" with examples*

SF1	Every physical object is made up of some number of component parts arranged in a particular 3-D **structure**. The objects of interest in physiology span all levels of organization from molecules and ions to organ systems.		
SF2	Biological objects interact with one another in a variety of ways that give rise to the **functions** carried out by a biological organism (respiration, energy production, internal transport, reproduction, etc.).		
SF3	Biological **structures** constrain the features of the **functions** that they generate (at every level of organization).		
	SF3.1	The arrangement of elements making up a tissue or organ (its **structure**) determines it **function**. Examples include:	
		SF3.1.1	Conduction of cardiac excitation
		SF3.1.2	The flow of blood through the heart and the heart valves
		SF3.1.2	Excitation-contraction coupling in skeletal muscle
	SF3.2	The physical dimensions (surface area, thickness - **structure**) are determinants of the flux of substances across a transport barrier (**function**). Examples include:	
		SF3.2.1	The alveolar-pulmonary capillary interface
		SF3.2.2	Capillary beds in all organs
		SF3.2.3	The intestinal mucosa (villi and microvilli) determines absorption of nutrients
	SF3.3	The 3-D **structure** of proteins determine their **function.** Examples include:	
		SF3.3.1	The 3-D **structure** of channels and transporters determines their specificity, permeability, and their **function** as gates
		SF3.3.2	The 3-D **structure** of enzymes determines their activity (**function**)
		SF3.3.3	Binding of H^+, O_2, and CO_2 to Hb alters its **structure** and thus its binding capacity for H^+, O_2, and CO_2 (**function**).
SF4	Changes in **function** can give rise to changes in the **structures** that generate them. Examples include:		
	SF4.1	Exercise changes fiber types in skeletal muscle	
	SF4.2	Effects of exercise and gravity on bone density	
	SF4.3	Effects of exercise on the heart	

No attempt has been made to validate this conceptual framework. See text for a fuller description of items SF3.1, SF3.2, SF3.3, and SF4.

"structure/function" will depend on the needs of the students taking a particular course.

The fact is that we know relatively little about what students understand about the concept of "structure/function" and whether they understand how to use it in thinking about physiological phenomena. An explicit understanding of what we mean by this concept is certainly a necessary starting point. Although some research about this has occurred (9), more research is clearly needed to provide the teaching community with information needed to make pedagogical decisions in the classroom.

I want to end with asking what do you mean by "structure/function" when you use this core concept in helping your students master physiology?

ACKNOWLEDGMENTS

I thank Jenny McFarland for reading several of the drafts of this paper and making many valuable suggestions that helped shape the arguments that I have presented.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author.

AUTHOR CONTRIBUTIONS

J.M. drafted manuscript; J.M. edited and revised manuscript; J.M. approved final version of manuscript.

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