

CURRICULUM
DEVELOPMENT AND ASSESSMENT

Physiology Core Concepts

Unpacking the homeostasis core concept in physiology: an Australian perspective

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Abstract

Australia-wide consensus was reached on seven core concepts of physiology, which included homeostasis, a fundamental concept for students to understand as they develop their basic knowledge of physiological regulatory mechanisms. The term homeostasis is most commonly used to describe how the internal environment of mammalian systems maintains relative constancy. The descriptor “the internal environment of the organism is actively regulated by the responses of cells, tissues, and organs through feedback systems” was unpacked by a team of three Australian Physiology educators into 5 themes and 18 subthemes arranged in a hierarchy. Using a five-point Likert scale, the unpacked concept was rated by 24 physiology educators from 24 Australian Universities for level of importance and level of difficulty for students. Survey data were analyzed using a one-way ANOVA to compare between and within concept themes and subthemes. There were no differences in main themes for level of importance, with all ratings between essential or important. *Theme 1: the organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis* was almost unanimously rated as essential. Difficulty ratings for unpacked concept themes averaged between slightly difficult and moderately difficult. The Australian team concurred with published literature that there are inconsistencies in the way the critical components of homeostatic systems are represented and interpreted. We aimed to simplify the components of the concept so that undergraduates would be able to easily identify the language used and build on their knowledge.

NEW & NOTEWORTHY The homeostasis core concept of physiology was defined and unpacked by an Australian team with the goal of constructing a resource that will improve learning and teaching of this core physiology concept in an Australian Higher Education context.

core concepts; higher education; homeostasis; physiology

INTRODUCTION

Homeostasis has been identified as one of the most important core physiology concepts by both educators and students (1, 2). In a survey of more than 100 physiologists from associate colleges to research-intensive institutions, “homeostasis” was ranked, together with “cell membranes,” as the

top two most important principles for physiology students to understand (1).

A review of Australian undergraduate degree-program curricula identified inadequate mapping of existing core concepts to subject learning outcomes within our Australian educational programs (3). The Delphi Method was undertaken by a group of Australian physiology educators from different

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universities brought together to form a “Task Force” with the aim of reaching a consensus on the core concepts of physiology that should be embedded into the Australian undergraduate physiology curriculum (4). In our Australian context, there was unanimous agreement from Task Force members and the broader physiology educator community that homeostasis was an essential core concept of physiology (4), consistent with published literature from the northern hemisphere (1).

Homeostasis is widely accepted as a central tenet of physiology and has been “unpacked” by physiology educators elsewhere (5, 6). There was consensus from Australian physiology educators that an appropriate descriptor for homeostasis is “the internal environment of the organism is actively regulated by the responses of cells, tissues, and organs through feedback systems” (4). Physiology educators who mapped learning outcomes within Australian physiology courses against homeostasis core concept keywords deemed that there was a considerable degree of misalignment with only 15% of learning outcome statements being deemed as fully related, 16% as “somewhat related,” and 69% “not related” (3).

Students can be confused about what homeostasis is, which physiological variables are regulated by homeostatic mechanisms, and which internal environments are maintained (7, 8). Students appear to particularly struggle with understanding the continuous signaling function of sensors within control systems (i.e., that they do not turn on and off like a switch depending on circumstances) and how the control center integrates incoming sensory information (9), such that some variables are prioritized over others. Indeed, some educators also have inconsistent views as to what constitutes homeostasis (8). In this paper, we attempted to come to a consensus regarding the defining features of homeostasis within our group of Australian educators.

Before advocating the use of the core concept theme and subtheme statements relating to homeostasis, there was a need to review and refine the concept statements to ensure they were appropriate for the Australian context. By better defining and unpacking the core concepts of homeostasis and gaining educator “buy-in,” we hope to facilitate and improve their inclusion and mapping within our Australian courses and provide a tool to educators to do so with consistency across our educational programs.

We therefore sought to evaluate the existing homeostasis concept statements and refine these with the intended purpose of aligning them with learning outcomes of our undergraduate programs. Our aim was to synthesize a framework to assist Australian educators teach the concept of homeostasis at a level easily understood by our undergraduate students and in context to their program of study. Ideally, this can also be used as a learning tool to assist students to conceptualize and apply the main themes and subthemes of the concept.

METHODS

Unpacking the Core Concept of Homeostasis

The team responsible for unpacking the core concept of homeostasis were the first three authors (E.A.H.B., V.G., and A.J. B) and meetings were facilitated by M.T. Collectively the team members have published more than 100 research articles relating to physiology, cell biology, and pharmacology, and

each has been teaching biomedical sciences for 20 yr or longer and has considerable experience with undergraduate curriculum design, development, and delivery. The team reviewed the themes and subthemes previously proposed by Michael et al. (5) and considered if these required restructuring to be “fit-for-purpose” in the Australian Higher Education context. This included whether the statements clarified important points required for students’ understanding and whether further unpacking and editing were required. The synthesized list of themes and subthemes was then rated by the survey participants (Task Force members) and further refined according to feedback.

Survey Participants

The unpacked themes and subthemes were entered into a Qualtrics survey and assessed by 25 physiology educators (the Task Force). Each of the survey participants work at different Australian Universities, with all Australian States and the Australian Capital Territory represented and with an average of 16.4 ± 7.2 yr of experience teaching physiology.

Survey

Survey participants were asked to rate the homeostasis themes and subthemes. A five-point Likert scale was used to determine, for each theme and subtheme statement, the level of importance for students to understand (1 = Essential, 2 = Important, 3 = Moderately Important, 4 = Slightly Important, and 5 = Not Important) and level of difficulty for student comprehension (1 = Very Difficult, 2 = Difficult, 3 = Moderately Difficult, 4 = Slightly Difficult, and 5 = Not Difficult). Survey participants were also provided an open-response field for their qualitative feedback on the validity of the statements. The “*n*” numbers in the results tables (Tables 1 and 2) represent the number of rating responses received for each theme and subtheme.

Statistical Analysis

Survey responses were analyzed with a one-way ANOVA to compare response data between and within themes and subthemes using SPSS. Linear correlation was undertaken using GraphPad Prism, and for all statistical tests, $P < 0.05$ was considered as significant.

RESULTS

The core concept of homeostasis with a descriptor approved by the Delphi process (4): “the internal environment of the organism is actively regulated by the responses of cells, tissues, and organs through feedback systems” was unpacked into five main themes. The five themes were as follows: 1) *theme 1: the organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis*; theme 2: *homeostatic mechanisms require internal sensors*; theme 3: *homeostatic mechanisms require a control center*; theme 4: *homeostatic mechanisms require targets called effectors*; and theme 5: *all homeostatic mechanisms utilize negative feedback*. Each theme was further unpacked into two to five lower tier subthemes. The 5 themes and 18 subthemes are outlined in Table 1. Twenty-four participants responded to the survey;

Table 1. Survey data for the level of importance for students to understand as rated by Task Force members

Themes	Average Importance	%Total Respondents That Rated as				
		1: Essential	2: Important	3: Moderately Important	4: Slightly Important	5: Not Important
1: The organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis.	1.04 ± 0.20	95.8	4.2	0	0	0
1.1: Key variables of the internal environment are kept stable by homeostatic mechanisms to sustain cell, tissue and organ function, these are known as regulated variables. If the regulated variables change too much, cells cannot function normally.	1.29 ± 0.55	75	20.8	4.2	0	0
1.2: The regulated variable may be kept within a very narrow range or within a much wider range, despite changes in the external environment. The maintained range is referred to as a set-point.	1.58 ± 0.58	45.8	50.0	4.2	0	0
1.3: To be classified as a homeostatic mechanism, 3 critical components are required: a sensor, a control center and an effector. Note that these components may be physically far from or near to each other in the body and can even exist in the same cell.	1.33 ± 0.48	66.7	33.3	0	0	0
1.4: Homeostatic regulatory mechanisms operate all the time to monitor and control the value of the regulated variable (they do not turn “on” or “off”; they are not like a “light switch,” they are like a “volume control”).	1.83 ± 0.87	41.7	37.5	16.6	4.2	0
1.5: Some variables remain within a normal range but do not have the critical components of a homeostatic mechanism (e.g., heart rate).	2.92 ± 1.28	16.7	20.8	29.2	20.8	12.5
2: Homeostatic mechanisms require internal sensors.	1.29 ± 0.46	70.8	29.2	0	0	0
2.1: Homeostatic mechanisms employ a variety of types of sensors such as chemoreceptors, mechanoreceptors and thermoreceptors.	1.58 ± 0.58	45.8	50.0	4.2	0	0
2.2: Regulated variables are constantly monitored by sensors.	1.54 ± 0.59	50.0	45.8	4.2	0	0
2.3: Sensors detect the magnitude of the regulated variable and generate an output signal that is proportional to the magnitude of the stimulus input to the sensor.	2.09 ± 0.79 (n = 23)	26.1	39.1	34.8	0	0
2.4: The output signal from the sensor is relayed to the control center.	1.78 ± 0.95 (n = 23)	43.5	43.5	8.7	0	4.3
3: Homeostatic mechanisms require a control center.	1.21 ± 0.66	87.5	8.3	0	4.2	0
3.1: The control center is part of the endocrine and/or the nervous system. More than one homeostatic mechanism can contribute to the regulation of a particular variable.	1.75 ± 0.68	37.5	50	12.5	0	0
3.2: The control center (often called an integrator) receives signals from the sensors and determines the difference between the sensor input and the set range.	1.50 ± 0.66	58.3	33.3	8.3	0	0
3.3: If the integrated input signal deviates from the set-point the control center will send output signals to effectors, increasing or decreasing activity.	1.38 ± 0.71	70.8	25	0	4.2	0
3.4: It is possible, in some circumstances, for the set-point to change (for example, body temperature in case of a fever).	2.25 ± 0.85	16.7	50	25.0	8.3	0
3.5: Homeostatic mechanisms can be overridden by the sympathetic nervous system.	2.42 ± 0.97	16.7	41.7	25.0	16.7	0
4: Homeostatic mechanisms require targets called effectors.	1.38 ± 0.58	66.7	29.2	4.2	0	0
4.1: Effectors are cells, tissues, or organs that receive the control center output.	1.46 ± 0.59	58.3	37.5	4.2	0	0
4.2: Effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure). Note that non-regulated variables are not directly sensed (i.e., there is no sensor for heart rate or stroke volume).	2.09 ± 1.08 (n = 23)	30.4	47.8	8.7	8.7	4.3
5: All homeostatic mechanisms utilize negative feedback.	1.50 ± 0.88	70.8	12.5	12.5	4.2	0
5.1: Negative feedback is a control mechanism that limits the response brought about by the effector once the regulated variable is within the set-point range.	1.43 ± 0.59 (n = 23)	60.9	34.8	4.3	0	0
5.2: Not all negative feedback systems are homeostatic (e.g., negative feedback control of appetite).	2.50 ± 1.32	20.8	45.8	8.3	12.5	12.5

Values are means ± SD or percent; n = 24 unless stated.

Table 2. Survey data for the level of difficulty for students to understand as rated by Task Force members

Themes	Average Difficulty	%Total Participants That Rated as				
		1: Very Difficult	2: Difficult	3: Moderately Difficult	4: Slightly Difficult	5: Not Difficult
1: The organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis.	4.13 ± 0.99	0	8.3	16.7	29.2	45.8
1.1: Key variables of the internal environment are kept stable by homeostatic mechanisms to sustain cell, tissue and organ function, these are known as regulated variables. If the regulated variables change too much, cells cannot function normally.	3.79 ± 1.14	0	16.7	25	20.8	37.5
1.2: The regulated variable may be kept within a very narrow range or within a much wider range, despite changes in the external environment. The maintained range is referred to as a set-point.	3.83 ± 0.96	0	8.3	29.2	33.3	29.2
1.3: To be classified as a homeostatic mechanism, 3 critical components are required: a sensor, a control center and an effector. Note that these components may be physically far from or near to each other in the body and can even exist in the same cell.	3.54 ± 0.93	0	12.5	37.5	33.3	16.7
1.4: Homeostatic regulatory mechanisms operate all the time to monitor and control the value of the regulated variable (they do not turn on or off; they are not like a light switch; they are like a volume control).	3.96 ± 0.86	0	4.2	25	41.7	29.2
1.5: Some variables remain within a normal range but do not have the critical components of a homeostatic mechanism (e.g., heart rate).	3.43 ± 0.79	0	8.7	47.8	34.8	8.7
2: Homeostatic mechanisms require internal sensors.	4.22 ± 0.60	0	0	8.7	60.9	30.4
2.1: Homeostatic mechanisms employ a variety of types of sensors such as chemoreceptors, mechanoreceptors and thermoreceptors.	3.70 ± 0.70	0	8.7	17.4	69.6	4.3
2.2: Regulated variables are constantly monitored by sensors.	4.09 ± 0.60	0	0	13.0	65.2	21.7
2.3: Sensors detect the magnitude of the regulated variable and generate an output signal that is proportional to the magnitude of the stimulus input to the sensor.	3.05 ± 0.90 (n = 23)	0	36.4	22.7	40.9	0
2.4: The output signal from the sensor is relayed to the control center.	3.91 ± 0.87 (n = 23)	0	4.5	27.3	40.9	27.3
3: Homeostatic mechanisms require a control center.	4.09 ± 0.85 (n = 23)	0	4.3	17.4	43.5	34.8
3.1: The control center is part of the endocrine and/or the nervous system. More than one homeostatic mechanism can contribute to the regulation of a particular variable.	3.43 ± 1.04 (n = 23)	0	17.4	43.5	17.4	21.7
3.2: The control center (often called an integrator) receives signals from the sensors and determines the difference between the sensor input and the set range.	3.22 ± 0.90 (n = 23)	4.3	8.7	56.5	21.7	8.7
3.3: If the integrated input signal deviates from the set-point the control center will send output signals to effectors, increasing or decreasing activity.	3.52 ± 1.04 (n = 23)	4.3	4.3	47.8	21.7	21.7
3.4: It is possible, in some circumstances, for the set-point to change (for example, body temperature in case of a fever).	3.57 ± 1.12 (n = 23)	4.3	13.0	26.1	34.8	21.7
3.5: Homeostatic mechanisms can be overridden by the sympathetic nervous system.	3.04 ± 1.02 (n = 23)	4.3	26.1	39.1	21.7	8.7
4: Homeostatic mechanisms require targets called effectors.	4.13 ± 0.97	0	8.7	13.0	34.8	43.5
4.1: Effectors are cells, tissues, or organs that receive the control center output.	4.09 ± 0.85	0	4.3	17.4	43.5	34.8
4.2: Effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure). Note that non-regulated variables are not directly sensed (i.e., there is no sensor for heart rate or stroke volume).	2.5 ± 0.96 (n = 23)	18.2	27.3	40.9	13.6	0
5: All homeostatic mechanisms utilize negative feedback.	3.74 ± 0.96	4.3	4.3	21.7	52.2	17.4
5.1: Negative feedback is a control mechanism that limits the response brought about by the effector once the regulated variable is within the set-point range.	3.45 ± 1.06 (n = 23)	4.5	13.6	27.3	40.9	13.6
5.2: Not all negative feedback systems are homeostatic (e.g., negative feedback control of appetite).	3.09 ± 0.97	13.6	0	50	36.4	0

Values are means ± SD or percent; n = 24 unless stated.

however, 2 participants did not provide responses to every survey question; therefore, “*n*” numbers for individual survey questions ranged from 22 to 24.

There was no difference in the mean importance rating for the five main concept themes, with each rated by individual participants as either Essential (Likert score 1) or Important (Likert score 2). Mean importance ratings for the five themes ranged from 1.63 to 1.82 (Table 1).

Theme 1: the organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis was ranked as the most important, rated as Essential (Likert score 1) by all but one of the survey participants (mean 1.04 ± 0.2 ; $n = 24$). The main concept *theme 5: all homeostatic mechanisms utilize negative feedback* was regarded as the least important of the 5 main themes but still received 16 ratings of Essential, 3 of Important, 3 of Moderately Important, and a single rating of Slightly Important (mean 1.50 ± 0.88 ; $n = 24$) (Table 1).

The majority (12 of 18) subthemes received average importance ratings, in the Important to Essential range. Six subthemes (*subthemes 1.5, 2.3, 3.4, 3.5, 4.2, and 5.2*) were rated slightly less important, but still in the Moderately Important to Important range (i.e., mean importance ratings between 2 and 3). Of these, *subtheme 1.5: some variables remain within a normal range but do not have the critical components of a homeostatic mechanism (e.g., heart rate)* was rated as the least important and there was a broad range of participant responses (i.e., mean importance rating of 2.92 ± 1.28). For three of the subthemes (i.e., *subthemes 1.5, 4.2, and 5.2*), the variability in the perceived level of importance exceeded 1 standard deviation from the mean (Table 1).

With regards to the educators’ perceived difficulty of the five main themes, mean difficulty ratings for *themes 1 to 4* were all within the Slightly Difficult to Not Difficult range (Table 2). Only the main concept *theme 5: all homeostatic mechanisms utilize negative feedback* received a mean difficulty rating less than 4 (3.74 ± 0.96 , in the Moderately to Slightly Difficult range). No statistical difference in the mean difficulty rating between themes and subthemes was detected.

Subthemes were rated across all five difficulty levels of the Likert scale, indicating a higher level of variation in participant perception of difficulty compared to the consistently rated main themes. There were six subthemes for which the variability in the perceived level of difficulty for students exceeded 1 standard deviation from the mean. These were *subthemes 1.1, 3.1, 3.3, 3.4, 3.5, and 5.1* (see Table 2 and Fig. 2). Only two subthemes were rated, on average, in the Not Difficult to Slightly Difficult category (i.e., mean ratings of 4 or more). The majority (15 of 18) of subthemes received mean difficulty ratings in the Slightly Difficult to Moderately Difficult range (i.e., mean ratings between 3 and 4). The only subtheme that received a mean difficulty rating less than 3 was *subtheme 4.2: effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure)*. This subtheme was regarded as the Most Difficult of all subthemes with a mean difficulty rating of 2.5 ± 0.96 .

A significant inverse relationship between survey participants’ perception of the importance and difficulty of the main theme and subtheme statements was found ($R^2 = 0.373$, $P = 0.002$) (see Fig. 3). This suggests that survey participants

generally viewed the most important themes and subthemes as relatively easy for students to comprehend.

Open-Response Feedback from Survey Participants

Survey participants (the Task Force members) also provided open-response comments relating to the theme and subtheme statements providing insight into whether any revisions to these statements were required to improve clarity. The feedback comments that queried or contested statements related mostly to *theme 1*, particularly *subtheme 1.5*, which is consistent with the variability in rating of this subtheme by survey respondents (Tables 1 and 2; Figs. 1, 2, and 3). The comments for *subtheme 1.5* related to further context required to clarify the statement. *Subtheme 1.5* was revised to include the following wording: *subtheme 1.5: some variables remain within a typical range of values for healthy mammals but do not have the critical components of a homeostatic mechanism (e.g., heart rate)*.

Theme 4, specifically *subtheme 4.2*, also received comments suggesting it could be further clarified to avoid confusion. Respondents were critical of the length of the subtheme and the example used, although there were contradictory viewpoints on the choice of example. These opposing views are consistent with the variability in rating of this subtheme by survey respondents for Importance and Difficulty (Tables 1 and 2; Figs. 1 and 2).

In general, feedback relating to the length and complexity of some of the subtheme statements led to rewording for clarification purposes. Additionally, the team further unpacked two of the themes into additional hierarchical levels. The suggested changes are reflected in the revised homeostasis themes and subthemes (Table 3), with notable addition of a third hierarchical level to *subtheme 1.2 (1.2.1: the maintained range is referred to as a set-point)* and *subtheme 4.2 (4.2.1: nonregulated variables are not directly sensed (i.e., there is no sensor for heart rate or stroke volume))*.

DISCUSSION

In this study, we aimed to define and validate a conceptual framework for homeostasis relevant for undergraduate physiology education in Australia. Acknowledging the broad nature of the term homeostasis, and what it could include, our team used a lens focused on three important considerations: 1) mammalian organismal physiology (i.e., not cellular); 2) negative feedback control of regulated variables critically required for stability of the extracellular compartment (and therefore life), for example, thermoregulation, plasma glucose regulation, and osmoregulation (8); and 3) adoption of the simplified engineering control model, that operationalizes the concept and identifies the essential components of homeostatic regulatory mechanisms: a sensor, control center and effector (8, 10). With such a model, sensors in the system provide continuous monitoring of the regulated variable. The control center integrates information relayed from the sensors and sends output (proportion to the magnitude of the deviation from the set point) to the effector (s) to return the variable to within the set-point range required for normal functioning of the body (8).

From the outset, our team recognized that a simplified engineering control model does not fully encapsulate the complex

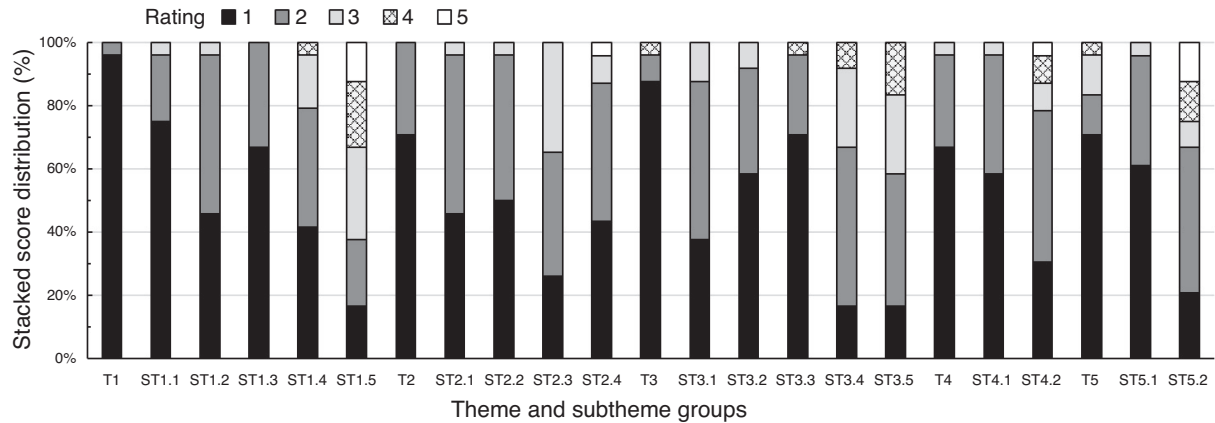


Figure 1. Percent stacked score distributions for Likert ratings of theme (T) and subtheme (ST) importance (1 = Essential, 2 = Important, 3 = Moderately Important, 4 = Slightly Important, and 5 = Not Important).

interaction of multiple feedback systems or the modification by higher control centers that contribute to the dynamic process of homeostatic regulation. In its simplest form, the engineering control loop neglects the sophisticated hierarchical control and feedback redundancy of homeostatic control mechanisms that result in a fine level of control and the flexibility to enable adaptation to changed circumstances and conditions. There was however agreement within our group that teaching using the analogy of an engineering control system (8) would assist our first-year and second-year undergraduate students form a basic understanding of the concept.

The revised descriptor for homeostasis and unpacked theme and subtheme statements (Table 1) considered by the Task Force members were similar to those presented by Michael et al. (5). However, a discussion between unpacking team members led to the simplification, rephrasing, and resequencing of theme and subtheme statements. First, the overall number of unpacked statements was decreased from 25 to 21, primarily by omitting *subthemes 1.1, 1.5, 2.4, and 4.7* as listed in Table 5.1 of Michael et al. (5). There was consensus within the unpacking team that these were not essential for an appropriate undergraduate understanding of the core concept of homeostasis. The team also agreed that it was logical

to first present the three critical components of a homeostatic mechanism before further unpacking the specifics of each component, as described in *subtheme 1.3: to be classified as a homeostatic mechanism, 3 critical components are required; a sensor, a control center and an effector* (see Table 1). We also replaced the concept of an integrator located within a control center (as mentioned in Table 5.1 in Ref. 8), with the simpler term “control center,” consistent with the simplified homeostatic control system model presented by Model et al. (8). In addition, we presented the components as main themes in a sequence consistent with the standard engineering model of a homeostatic control system.

The Task Force group rated the five main concept themes as very important and not particularly difficult for students to understand. This is likely a welcome finding for educators and students as it suggests the most important key principles of homeostasis are the easiest to explain and conceptualize. The five main concept themes relate to the existence of regulatory mechanisms that maintain the internal environment of an organism (T1); the components of homeostatic regulatory mechanisms; sensors, control centers, and effectors (T2, T3, and T4); and the importance of negative feedback control loops (T5).

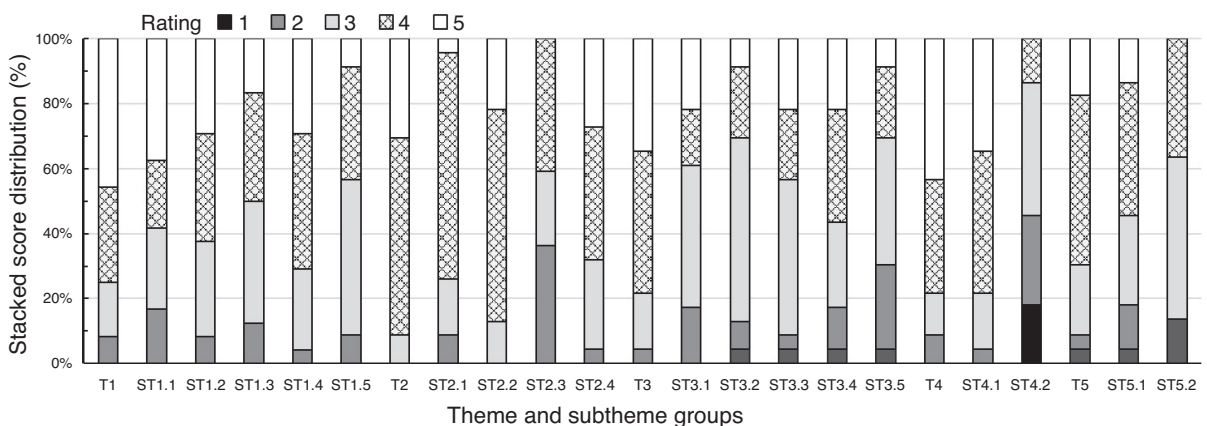


Figure 2. Percent stacked score distributions for Likert ratings of theme (T) and subtheme (ST) difficulty (1 = Very Difficult, 2 = Difficult, 3 = Moderately Difficult, 4 = Slightly Difficult, and 5 = Not Difficult).

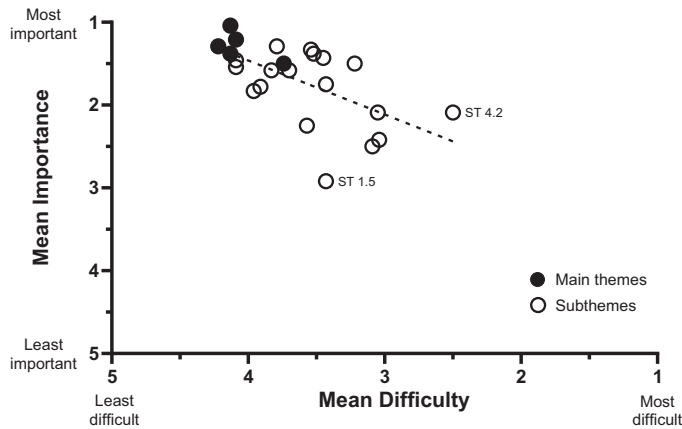


Figure 3. Mean Likert rating for Importance as a function of mean rating for Difficulty, for the main themes (closed circles) and subthemes (open circles) (Importance: 1 = Essential, 2 = Important, 3 = Moderately Important, 4 = Slightly Important, and 5 = Not Important; Difficulty: 1 = Very Difficult, 2 = Difficult, 3 = Moderately Difficult, 4 = Slightly Difficult, and 5 = Not Difficult). A significant linear correlation was found between these 2 parameters (dashed line, $R^2 = 0.373$, $P = 0.002$). *Subtheme 4.2 (ST 4.2)*, determined to be the most difficult of all subthemes and *subtheme 1.5 (ST 1.5)*, regarded as the least important, are annotated.

Compared to the main themes, there was considerably more inconsistency in participant ratings of the importance and difficulty of the subthemes. *Subtheme 1.5: some variables remain within a normal range but do not have the critical components of a homeostatic mechanism. (e.g., heart rate)* was viewed as the least important, and the variability between respondents in their evaluation of importance was one of the largest. Respondents also rated this subtheme as one of the most difficult for students to understand.

The contention regarding which variables meet the criteria for a homeostatically regulated variable has been previously discussed (8). The unpacking team adopted the same stance as Model et al. (8) that homeostatically regulated variables are limited to those regulated by a process that involves all the components of the engineering control model, including a direct physiological sensor for the variable. It is possible that some educators have a more relaxed view of what constitutes a homeostatically regulated variable and include variables that remain in a typical range (such as hormone concentrations, heart rate, and metabolic waste products). *Subtheme 1.5* makes the distinction that although some variables remain relatively constant (often involving negative feedback processes), the body does not possess a physiological sensor for directly detecting them and therefore are not maintained by a system that meets the definition of a homeostatic mechanism. Some respondents may have viewed this definition of what constitutes a homeostatically regulated variable as more, or less, important than others depending on their own conceptual understanding, and this was reflected in the open-response section of the survey.

Subtheme 3.4: it is possible, in some circumstances, for the set-point to change (for example, body temperature in case of a fever) and *subtheme 3.5: homeostatic mechanisms can be overridden by the sympathetic nervous system* were included in the original set of unpacked statements to emphasize the dynamic, adaptive nature of homeostatic regulatory systems

and that set points can fluctuate in response to internal and external factors. It was decided not to include more detail regarding the higher levels of control, such as described by Goodman (11) by which the set point (or more accurately the operating range) of the negative feedback regulation can be adjusted or even overridden. *Subthemes 3.4* and *3.5* were not perceived to be as important as others (both ranking in the bottom 4 for importance for students to understand). There was also a high degree of variability when it came to perceived difficulty for students to understand (more than 1 SD from the mean), and *subtheme 3.5* was rated as one of the most difficult for students to understand. This may have stemmed from an unease with the singling out of the sympathetic nervous system as a component that can “override” homeostatic mechanisms, especially given the role of the sympathetic nervous system in the maintenance of several homeostatically regulated variables. In response to qualitative feedback, this subtheme was edited to *subtheme 3.5: some homeostatic mechanisms can be overridden by the sympathetic nervous system*. This subtheme may have been perceived to deviate from, or even contradict, the simple negative feedback schema described within the rest of the unpacked concept statements (and in many physiology texts).

Survey participants rated *subtheme 4.2: effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure)* as being the most difficult for students to understand. This subtheme relates to the action of effectors to adjust nonregulated variables via physical or chemical responses which in turn adjust the regulated variable. Some respondents were critical of the length of the subtheme and a couple explained that they were not confident of the use of stroke volume as an example of a non-homeostatically regulated variable. Although there was considerable variation in difficulty rating for *subtheme 4.2*, all respondents recognized the importance of students understanding this point, rating it as either Essential, Important, or Moderately Important (Table 1). In the revised set of statements, a third tier was added to *themes 2* and *4*, which was in response to feedback from Task Force members (via the open-response section of the survey) that this would improve clarity (Table 3).

There was also a high degree of variability with regard to perceived importance of *subtheme 5.2: not all negative feedback systems are homeostatic (e.g., negative feedback control of appetite)*. This may have been because this statement does not directly relate to what homeostasis is, but rather emphasizes that the existence of negative feedback in a regulatory system does not always mean that the variable (or variables) in that system is (are) being homeostatically regulated. In the open-response feedback comments, it was apparent that two participants were uneasy with the suggestion that appetite was not a homeostatically regulated variable.

As we unpack concepts to increase student understanding, there is a risk of oversimplification and reductionism to the extent that much of the complexity and sophistication of the biological system being described is lost. Concern regarding the oversimplification of homeostasis as a concept has been expressed previously (12, 13). It could be argued that

Table 3. Revised homeostasis unpacked core concepts based on open-response feedback

Themes
<p>1. The organism has regulatory mechanisms to maintain a relatively stable internal environment, a process known as homeostasis.</p> <p>1.1. Key variables of the internal environment are kept stable by homeostatic mechanisms to sustain cell, tissue and organ function, these are known as regulated variables. If the regulated variable changes too much, cells cannot function normally.</p> <p>1.2. A physiological variable may be kept within a specific range, despite changes in the external environment.</p> <p>1.2.1. The maintained range is referred to as a set-point.</p> <p>1.3. To be classified as a homeostatic mechanism, 3 critical components are required: a sensor, a control center and an effector.</p> <p>1.4. Homeostatic regulatory mechanisms operate all the time to monitor and control the value of the regulated variable (they do not turn on or off like a light switch, they are like a 'volume control').</p> <p>1.5. Some variables remain within a typical range of values but do not have the critical components of a homeostatic mechanism. (e.g., heart rate).</p> <p>2. Homeostatic mechanisms require internal sensors.</p> <p>2.1. Homeostatic mechanisms employ a variety of types of sensors such as chemoreceptors, mechanoreceptors and thermoreceptors.</p> <p>2.2. Regulated variables are constantly monitored by sensors.</p> <p>2.3. Sensors monitor the magnitude of the regulated variable and generate an output signal that is proportional to the difference from the set-point.</p> <p>2.4. The output signal from the sensor is relayed to the control center.</p> <p>3. Homeostatic mechanisms require a control center.</p> <p>3.1. The control center is part of the endocrine and/or the nervous system.</p> <p>3.2. More than one homeostatic mechanism can contribute to the regulation of a particular variable.</p> <p>3.3. The control center receives signals from the sensors and determines the difference between the sensor input and the set-point.</p> <p>3.4. If the integrated input signal deviates from the set-point the control center will send output signals to effectors, increasing or decreasing the activity of effectors.</p> <p>3.5. It is possible, in some circumstances, for the set-point to change (e.g., body temperature in case of a fever).</p> <p>3.6. Some homeostatic mechanisms can be overridden by the sympathetic nervous system.</p> <p>4. Homeostatic mechanisms require targets called effectors.</p> <p>4.1. Effectors are cells, tissues, or organs that receive the control center output.</p> <p>4.2. Effectors adjust non-regulated variables (e.g., stroke volume) via physical or chemical responses (e.g., contraction of heart muscle) to adjust the regulated variable (e.g., blood pressure).</p> <p>4.2.1. Non-regulated variables are not directly sensed (i.e., there is no sensor for heart rate or stroke volume).</p> <p>5. All homeostatic mechanisms utilize negative feedback.</p> <p>5.1. Negative feedback is a control mechanism that limits the response brought about by the effector once the regulated variable is within the set-point range.</p> <p>5.2. Not all negative feedback systems are homeostatic (e.g., negative feedback loops are involved in regulating the concentration of cortisol in the plasma, but plasma cortisol concentration is not regulated via a homeostatic mechanism).</p>

our unpacked concept themes and subthemes do not adequately address either feedforward or higher order control of homeostatic regulation. Feedforward regulation is a mechanism by which homeostasis is modified and maintained as part of the behavioral response to environmental stimuli. For example, blood pressure, cardiac output, and skeletal muscle blood flow increase as part of a defense reaction, when exposed to potential danger or exercise. The importance of these sophisticated subcomponents of homeostasis is potentially undermined by using a reductionist set of statements to attempt to describe homeostasis. However, our team agreed that the revised set of theme and subtheme statements adequately emphasize the central principles and key components of homeostasis at a level that is appropriate for an undergraduate student needing to grasp the main points. It is also possible that educators can expand and evolve the statements as appropriate for different learning contexts.

It is necessary to acknowledge the limitations of our study in asking academics to evaluate undergraduate students who would find a concept theme or subtheme difficult or easy. It is possible that educators may assume that a concept statement is simple or straightforward, when in fact students may find it difficult or confusing. However, based on our course assessment information, we likely have a reasonably accurate view of what students find or perceive to be difficult. It is also worthy of note that students themselves may not have the metacognition

required to identify the areas of difficulty (i.e., they could think they understand correctly when they do not). Future studies could include a survey of current undergraduate student opinion on the perceived difficulty of the statements. This was however outside the scope of the current study in which the aim was for educators to reach a consensus on the wording of the themes and subthemes of the concept.

In conclusion, this study acknowledges the work of previous authors seeking a unified approach to the core concept of homeostasis. We pay homage to the concept originally proposed by Claude Bernard and later evolved by Walter Cannon who coined the term homeostasis and Norbert Wiener whose mathematical analysis of feedback control in biological systems introduced negative feedback to the concept (cited in Ref. 14). Supported unanimously by experienced physiology educators from around Australia, we adopted and unpacked homeostasis as a core concept of physiology. We have reviewed, defined, and validated a new set of homeostasis themes. These new statements will support undergraduate students learning physiology, specifically homeostasis, to meet the learning outcomes of physiology programs in Australian Higher Education Institutions.

DATA AVAILABILITY

Data will be made available upon reasonable request.

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DISCLOSURES

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

AUTHOR CONTRIBUTIONS

A.H., D.H.H., L.L., and K.T. conceived and designed research; E.A.H.B., V.G., A.J.B., M.T., and Task Force performed experiments; A.H. analyzed data; E.A.H.B., V.G., A.J.B., M.T., and A.H. interpreted results of experiments; E.A.H.B., V.G., A.J.B.,

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