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Unpacking the 'Movement of Substances' Core Concept of Physiology by an Australian team.

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Author Contributions: K.T., A.H., D.H., and L.L. conceived and designed the research; A.H. analyzed data and prepared tables; D.B., T.U., N.M. A.H. and K.T. drafted, edited and revised the manuscript. *D.B., T.U., and N.M. contributed equally to this work. The Task Force validated the core concept.

Running title: Unpacking the 'Movement of Substances' Core Concept

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ABSTRACT

Australia-wide consensus was reached on seven core concepts of physiology. The ‘Movement of Substances’ core concept with the descriptor ‘the movement of substances (ions or molecules) is a fundamental process that occurs at all levels of organisation in the organism’, was unpacked by a team of three Australian Physiology educators from the Delphi Task Force into hierarchical levels. There were ten themes and twenty-three sub-themes arranged in a hierarchy, some three levels deep. Using a five-point Likert scale, the unpacked core concept was then rated for level of importance for students to understand (ranging from 1=Essential to 5=Not Important) and level of difficulty for students (ranging from 1=Very difficult to 5=Not difficult) by the twenty-three physiology educators from different Australian universities, all with a broad range of teaching and curriculum experience. Survey data was analyzed using a one-way ANOVA to compare between and within concept themes. The main themes all were rated on average as important. There was a wide range of difficulty ratings and more variation for this concept compared with the other core concepts. This may in part to be due to the physical forces such as gravity, electrochemistry, resistance, thermodynamics that underpin this concept, which in themselves are inherently complex. Separation of concepts into sub-themes can help prioritize learning activities and time spent on difficult concepts. Embedding of core concepts across curricula will allow commonality and consistency between programs of study and inform learning outcomes, assessment and teaching and learning activities.

New & Noteworthy: This manuscript unpacks the core concept of the 'Movement of Substances' within the body, with the aim to produce a resource that will help guide the teaching of physiology at tertiary education institutes in Australia. The concept introduces fundamental knowledge of the factors that drive substance movement, and then applies them in physiological contexts.

Keywords: Physiology, core concepts, gradients

INTRODUCTION

It is well established that university educators need to encourage and support students to adopt deep approaches to their learning (1, 2, 3). A core concept or 'big idea' is defined by Michael and McFarland as "essential to the understanding and practice of a discipline, the mastery of which results in enduring understanding and ability to address novel problems across the discipline" (4). Establishing core concepts for physiology education may benefit students approaches to learning as well as provide a framework that can be adopted by institutions teaching physiological theory and practice in Australia. Moreover, the inclusion of a defined set of core concepts in a discipline, and then teaching to these core concepts, can be vital in meeting criteria for clinical accreditation, or gaining entry into a post-graduate course, or meeting the requirements of a job description. Currently in Australia, there are several accredited clinical education programs that require potential applicants to have, at a minimum, an undergraduate background in the biological sciences, and some more specifically require a physiology background such as the Australian Council for Clinical Physiologists.

The development of core concepts for physiology education began over 20 years ago using several physical principles as 'models' to help students understand physiological mechanisms (5). This work was a springboard for the description of fifteen core concepts of physiology described by Michael and McFarland (6), which later prompted a group of Australian educators (Task force) to reach consensus on seven core concepts of physiology that could be consistently embedded as 'big ideas' in the Australian Higher Education context (7). These concepts included 'Physiological Adaptation', 'Integration', 'Homeostasis', 'Structure and Function', 'Movement of Substances', 'Cell Membrane', and 'Cell-Cell Communication'. Through the Delphi consensus model, the core concept of the '*Movement of Substances*', and its descriptor, was considered as an essential concept in physiology with over 80% agreement from Task force members and the broader physiology educator community Australia-wide (7).

Aside from informing and directing curriculum design (8), there are numerous benefits and applications of core concept tools in physiological education. These include outlining a hierarchical structure of key components that help to explain the discipline (9); communicating learning outcomes (10); providing a scaffold which enables students to construct their own knowledge (11, 12); minimising surface approaches to learning such as rote memorization (13); and helping students to learn new material and make predictions based on their comprehension of a core concept (14).

This paper describes the unpacking of the core concept '*Movement of Substances'* and its descriptor '*The movement of substances (ions or molecules) is a fundamental process that occurs at all levels of organisation in the organism*' into themes and sub-themes, which were then validated with respect to their importance for undergraduate student understanding, as well as their perceived level of difficulty for students, by physiology educators from 23 Australian universities.

METHOD

The method as follows was adapted from that of Michael and co-workers (10).

Unpacking Process

A sub-group of three academics (DB, TU, NM) from three different Australian universities was established and assigned by the project lead (KT) the task of unpacking this core concept and its broader descriptor '*the movement of substances (ions or molecules) is a fundamental process that occurs at all levels of organisation in the organism'*. Each of the 3 academics had more than 8 years' experience teaching physiology at the senior lecturer level, each had taught physiology at more than one tertiary institution, and each was a coordinator of a physiology-embedded program.

The sub-group met online to discuss and develop the themes and sub-themes for this core concept. Several rounds of editing were undertaken to construct a hierarchical framework.

Survey participants

The unpacked themes and sub-themes were entered into a Qualtrics survey (KT) and a link sent out to 25 physiology educators who comprised the Task force participating in the Delphi protocol (7), of which 23 completed the survey. Each of the participants work at a different Australian university, with all Australian States and the Australian Capital Territory represented. All respondents have been highly engaged in undergraduate physiology teaching and curriculum development, all have a Postdoctoral qualification, and all have experience teaching at the Senior Lecturer level or higher.

Survey

Survey respondents were asked to rate the themes and sub-themes on a 5-point Likert scale for level of importance for the students to understand (1=Essential, 2=Important, 3=Moderately Important, 4=Slightly Important and 5=Not Important) and level of difficulty for students (1=Very Difficult, 2= Difficult, 3=Moderately Difficult, 4=Slightly Difficult and 5=Not Difficult). The themes and sub-themes are shown below in Table 1:

Table 1: **Core concept themes and sub-themes**

1.	Substances can be in gas, liquid (dissolved or colloid), or solid form.
2.	The movement of substances within the body involves physical principles.
3.	Substances move through the body, either within the same compartment, or between different compartments.
3.1	Compartments can be extracellular or intracellular.
3.2	Compartments vary in shape and size.
3.3	Compartments can be fluid or gas filled.
4.	The movement of substances can be an active or a passive process.
4.1	Passive movement involves substances moving down a concentration or pressure gradient, governed by the physical principles driving equilibrium.
4.2.1	Active movement requires energy to move substances: Up a concentration or pressure gradient.
4.2.2	Active movement requires energy to move substances: Within a tube against a resistance.
4.3	For electrically charged substances, the electrical gradient must also be considered, with similar charges repelling, and opposite charges attracting.
5.	Multiple gradients can act on a substance simultaneously.
5.1	The sum of the gradients is the net force driving movement of the substance.
6.	To move within or between compartments, substances must move against various levels and forms of resistance.
6.1	Resistance can be physical or electrical.
6.1.1	Charged or polar substances cannot easily move through non-polar membranes.
6.1.2	Other characteristics, such as size of the substance also affect its movement.
6.1.3	Permeability is a measure of how easily a substance moves through a barrier. Barrier permeability affects the rate of transport.
6.1.4	Substances moving within a fluid experience physical resistance.
6.1.5	Fluid moving through a compartment experiences physical resistance.
7.	The rate of substance movement is determined by the forces acting on the substance and the resistance to movement (along with other physical principles such as temperature).
8.1	Transcellular: between compartments either side of a membrane, moving through cells.

8.2	Transmembrane: between the cellular and extracellular compartments.
8.3	Paracellular: between compartments either side of a membrane, moving around cells.
8.4	Luminal: movement within the same compartment.
9.	Transcellular transport can involve the movement of solutes through membrane-bound protein channels, pores or carriers, and pumps. These transport mechanisms can involve simple or facilitated diffusion or secondary active transport.
9.1	The transport of substances is also influenced by proteins (e.g. enzymes/protein carriers within blood).
10.	Substance transport also includes a number of forms of bulk transport.
10.1	Vesicular transport across a membrane (e.g. Endocytosis, exocytosis, phagocytosis...).
10.2	Movement of fluid, gas or solids along a compartment (e.g. peristalsis, ventilation).
10.3	Cell-guided flow (e.g. cilia, flagella).
10.4	Secretions (exocrine, endocrine, fluid).

Statistical Analyses

Importance and difficulty ranking of core concept themes and sub-themes are reported as mean ± standard deviation. Statistical differences in survey responses were analyzed using a one-way ANOVA on Ranks a Kruskal-Wallis Test, with Dunn's post-hoc analysis, and Bonferroni correction for multiple comparisons, to compare between and within concept responses. A Kolmogorov-Smirnov test was performed to determine the distribution of the results. Statistical analysis was performed in SPSS version 28.0.1 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p<0.05$.

RESULTS

All major themes were judged to be between Essential and Important (ranging from 1.3 to 1.89) for physiology students to understand, as were 13 of the 23 sub-themes. The remaining sub-themes were ranked between Essential and Moderately Important (Figure 1A).

There were minimal differences between the ranking of importance across the major themes, with the only significant difference showing theme 4 ranking more important than theme 10 ($p=0.035$, not shown). However, when major themes and subthemes were grouped together, theme 4 was ranked significantly more important than themes 3, 6, 8, 9, and 10 (Figure 2A).
In relation to the level of difficulty, the majority of themes and sub-themes were ranked Moderately to Slightly difficult (mean difficulty 3.43, Figure 1B), with only 4 of the 32 themes/sub-themes ranked as Difficult for students to understand (Figure 1B). There was more variation in difficulty ratings, than in importance ratings, as demonstrated in Figure 2B. When themes/subthemes were grouped, theme 5, multiple gradients can act on a substance simultaneously, was rated more difficult (mean 2.59) than all other themes ($p<0.05$, Figure 2B), with the exception of theme 7, which was the only other theme rated within the Difficult range (mean 2.91). Themes and subthemes 1, 3, 3.1, 3.2 and 3.3 were considered significantly easier than all other themes ($p<0.05$), both judged to be within the Slightly Difficult range (4.48 and 4.20, respectively, Figure 1B).

Feedback comments were provided on 8 of the 32 sub-themes, all with a relatively consistent narrative. Comments on early themes 1-7 suggested the addition of physiological examples to make the themes clearer or that there was significant overlap with other core concepts. Comments on themes further down the hierarchy primarily suggested re-structuring the themes to remove examples, or to merge themes, such as merging theme 8 with theme 3, for the purpose of simplicity.

Figure 1.

Figure 2.

Following analysis of reviewer rankings and feedback comments, a final revised table of themes and sub-themes was developed by the sub-group (Table 2). This final table was not reviewed by the Task-force members, and has not undergone subsequent analysis of these themes and subthemes with respect to level of importance and difficulty for students. Several reviewers suggested merging Themes 3 and 8, and Themes 5 and 7. As a result, a simplified version of Theme 9 in the original table is now Theme 7. The decision to simplify Theme 9 resulted from several comments that the movement of solutes through membrane transport mechanisms would largely be covered in other Core Concepts, namely 'Cell-Cell communication', and the 'Cell Membrane'. Theme 10 and its sub-themes in the original table were also simplified into one major theme, Theme 8, in the revised table following several comments that the sub-themes of Theme 10 were too specific.

Table 2: Revised themes and sub-themes incorporating reviewer feedback.

Revised Core concept themes and sub-themes
1. Substances can be in gas, liquid (dissolved or colloid), or solid form.
2. The movement of substances within the body involves physical principles.
3. Substances move through the body, either within the same compartment, or between different compartments.
3.1 Compartments can be extracellular or intracellular.
3.1.1 Movement between the intracellular and extracellular environment is referred to as Transmembrane movement.
3.1.2 Movement between extracellular compartments, which involves transmembrane movement, is referred to as Transcellular movement.
3.1.3 Movement between extracellular compartments, which *does not* involve transmembrane movement, is referred to as Paracellular movement.
3.1.4 Movement within a compartment is referred to as Luminal movement.
3.2 Compartments vary in shape and size.

3.3 Compartments can be fluid or gas filled.
4. The movement of substances can be an active or a passive process.
4.1 Passive movement involves substances moving down a concentration or pressure gradient, governed by the physical principles driving equilibrium.
4.2 Active movement requires energy to move substances up a concentration or pressure gradient, or against a resistance.
4.3 For electrically charged substances, the electrical gradient must also be considered, with similar charges repelling, and opposite charges attracting.
5. Multiple gradients can act on a substance simultaneously. The sum of the gradients is the net force driving movement of the substance.
6. To move within or between compartments, substances must move against various levels of physical or electrical resistance.
6.1 Charged or polar substances cannot easily move through non-polar membranes, which act as a barrier.
6.2 Other characteristics, such as size of the substance, and temperature of the environment also affect its movement.
6.3 Permeability is a measure of how easily a substance moves through a barrier. Barrier permeability affects the rate of movement.
6.4 Substances moving within a fluid experience physical resistance.
6.5 Fluid moving through a compartment experiences physical resistance.
7. Transmembrane or luminal transport of substances is also influenced by proteins (e.g. enzymes/protein carriers within blood).
8. Substance movement in the body can involve complex physiological transport processes such as endocytosis, exocytosis, receptor-substrate movement, phagocytosis, peristalsis, ventilation, cilia or flagella movement, etc…), which cannot be easily understood based on physical principles alone.

DISCUSSION

The themes generated for the *Movement of Substances* core concept were influenced by the work of Michael and colleagues (15) who originally unpacked the core concept termed '*Flow Down Gradients*'. Using a 4-phase Delphi method, a Task force of physiology educators from 25 Australian Institutions agreed to change the original terminology from '*Flow Down Gradients*' to '*Movement of Substances'* (7). The concept '*Movement of Substances*' was chosen as it encompasses active movement and more complex forms of physiological movement such as endocytosis, whereas the concept '*Flow Down Gradients'* conjures themes regarding passive movements and their resistance only.

Whilst there is considerable overlap between '*Flow Down Gradients'* and '*Movement of Substances*', there are also some differences. There are 5 themes and 12 sub-themes for the work conceptualizing '*Flow Down Gradients*' (15), whereas there are 8 themes and 11 sub-themes under our '*Movement of Substances'* core concept (Table 2). Our sub-group specifically detailed where substances move, for example, within the same compartment or different compartments, as well as providing the necessary nomenclature for describing that movement, for example, transmembrane movement or transcellular movement. In contrast to the work of Michael and colleagues (15) who outlined that flow occurs due to differences in energy gradients between two points, our work specifically outlined that movement of substances can be both a passive process governed by physical principles driving equilibrium, and an active process requiring energy to move substances against gradients or resistance.

The framework for the '*Movement of Substances'* core concept started with relatively broad-scoping, physio-chemical themes that had minimal reference to biology, indicative of threshold concepts, or what Modell (4) called a 'general model'. It is expected that much of the content in these themes may already be familiar to the student, making it easier to adapt this knowledge to the application of physiology. These themes were subsequently incorporated into a physiological context in themes and sub-themes further down the hierarchy. This approach to the concept was preferable because, with the exception of a few specialized instances, the factors governing substance movement through fluids are not specific or unique to physiology, but instead apply to any physical system. The sub-group authors were of the opinion that this approach would ultimately provide a foundation where learners could reflect and build on these physical principles with respect to physiology, in alignment with a constructivist paradigm that fosters deeper approaches to learning (1). Many of the principles are driven by thermodynamics, and equations governing substance movement in the body which stem heavily from engineering, physics and chemistry such as Fick's Principle, Fick's Law, Starling's equation, Henry's law, Bohr's equation, Reynaud's number, Laplace's law, Poiseuille's equation, and even Ohm's law. Indeed Modell's (5) work using general models to help students understand physiology also drew from physical principles. Other core concepts in physiology, such as *Homeostasis*, are likely to involve themes that are more specific to physiological phenomena or structures. The rationale for our approach is also consistent with Michael and McFarland's (4) revised change to the original physiological core concepts in which 'causality' and 'physics/chemistry' were combined to form a new concept entitled 'physical properties of matter' with the explanation that several physical properties help to explain important physiological observations.

Given the physical nature of this concept, perhaps unsurprisingly, when the themes were reviewed by the wider Task force group, a significant number commented that the early themes lacked a clear relation to specific areas of the body, or that there was significant cross-over with themes within other core concepts such as *Cell Membrane*, where there is an overlap of the fundamental principles of transport. This may help to explain why, despite '*Movement of Substances'* being one of 7 core concepts adopted by an Australian Delphi consensus (7), academic rating of the original USA-derived 15 core concepts (6) against the learning outcomes from units comprising physiology majors across 18 Australian universities, revealed '*Flow down gradients'* listed at only number 13 by eight academic raters (16). However, the sub-group were of the opinion that this reflected the broad-scope of this core concept and the approach to the framework, where it is likely that many of the presented themes could be applied to specific areas of physiology, resulting in overlap with other core concepts, in turn leading the reviewer to propose a specific physiological example of the theme for clarity. In addition, the '*Movement of Substances'* core concept and its relation to the other core concepts or the curriculum was not discussed prior to the rating of the importance and difficulty by the wider Task force. Michael and McFarland (6) reported comments such as, overlapping themes or an unclear framework from respondents to their '*Flow Down Gradients*' core concept, noting that this reflected that respondents were not presented with a description of where the core concept sat in the overall structure of learning.

Another common view of the Task force group was that themes could benefit from examples, or that the physical principles should be stated and defined. Michael and colleagues (15) included specific examples in their core concept *Flow down gradients* by way of providing an application to physiological systems. The sub-group considered detailing the physical principles within the themes, however ultimately decided that there are far too many to include all, and that the use of examples risked narrowing the focus of the theme and excluding content, or increasing the overlap of this core concept with other core concepts. It would also likely detract from the constructivist approach of the framework. Therefore, the use of examples to illustrate the movement of substances was minimized, in favour for an approach where the content stayed true to the broad physical principles underpinning substance movement, thus being applicable to a broader audience than physiology specifically. The later themes (Themes 9 and 10 from Table 1) included examples of substance physiology/cellular processes, because the majority of these forms of substance movement were specific to physiology and could not easily be explained via the use of physio-chemical principles alone.

Analysis of the survey data revealed some interesting findings. 'The movement of substances can be an active or a passive process' (theme 4) was considered to be statistically more important than themes 3, 6, 8, 9 and 10. This theme and its sub-themes have widespread applicability in all body systems and levels of organisation. This theme is also foundational for themes 3, 6, 8, 9 and 10, which further explains its importance as a concept in physiology education.

Themes and subthemes 1, 3, 3.1, 3.2 and 3.3 were considered significantly easier than all other themes in terms of level of difficulty. These themes and sub-themes address concepts that may be considered as implicit, or assumed knowledge taught in secondary school, and therefore not as important.

The theme 'Multiple gradients can act on a substance simultaneously' and the theme 'The rate of substance movement is determined by the forces acting on the substance and the resistance to movement (along with other physical principles such as temperature)' were both rated more difficult than all other themes. These findings are consistent with the work of Michael and colleagues (15) who outlined a number of topics that are points of confusion for students. This included failure to recognize downstream 'energy' in a gradient, disregard for the presence of multiple gradients that determine flow, difficulties in identifying that molecules move independently of one another, and neglecting to take into consideration the various forms of resistance that oppose flow (15). The revised '*Movement of Substances'* themes and sub-themes (Table 2) may help to provide further clarity for educators and students with respect to these points of confusion. For example, we have used the term equilibrium when referring to passive movement of substances down pressure or concentration gradients thereby implying downstream 'energy'. We have also emphasized the various forms of resistance that oppose flow including polarity and size of substances, temperature of the environment, barrier permeability, and fluid and compartment physical resistance.

Although certain themes and sub-themes for this core concept were perceived to be more difficult than others for students, as perceived by educators (Figure 2), actual student difficulty has not as yet been validated. Both Modell (5) and Kutchai (17) acknowledge that tertiary students find physiology challenging as it is based on physics, chemistry and mathematics. Student perspectives regarding which themes and sub-themes are considered easy or difficult is a future research aim of the Task Force.

CONCLUSION

We have provided physiology educators with a framework for teaching the core concept '*Movement of Substances*'. As per the work of others in this area (10), the unpacked core concept is not a prescriptive learning tool that requires memorization of facts, but rather is a guide to understanding how substances move in physiological systems. Moreover, a didactic explanation of each of the themes and sub-themes presented in this core concept, as was provided by Michaels and colleagues (15), has not been provided here because there is significant overlap between the themes presented previously (6), and those in this project. The primary differences in our approach and that of Michaels and colleagues (15) has been the inclusion of active transport mechanisms, and a definition of different compartments in our framework, which we believe adds clarity to students' understanding of how substances move within the body.

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Acknowledgement: We would like to thank the extended Task force members who validated the unpacked core concept: Anthony Bakker, Elizabeth Beckett, Melissa Cameron, Julia Choate, Lisa Chopin, Matthew Cooke, Suzanne Estaphan, Sarah Etherington, Voula Gaganis, Andrew Moorhouse, Tamara Paravicini, Ben Perry, Chris Scott, Gabrielle Todd, and Glenn Wadley.

Funding: This research was partially funded by The Physiological Society UK.

LEGENDS

Figure 1. A) The Mean (+/-StDev) rating of importance of the major themes (solid black circles) and sub-theme (empty circles) as rated by Task force members (n=23) for *Movement of Substances* core concept. B) The Mean (+/-StDev) rating of difficulty of the major themes (solid black circles) and sub-theme (empty circles) as rated by Task force members (n=23) for *Movement of Substances* core concept. *Theme 8.0 did not incur a rating as this was introduced as a theme after the peer-review process due to feedback from reviewers.*

Figure 2. A): The percent ratings of importance of the major themes, sub-themes, and 'grouped' themes as determined by Task force members (n=23) for the *Movement of substances* core concept. Significant differences between the grouped themes are shown above each plot. B) The percent ratings of difficulty of the major themes, sub-themes, and 'grouped' themes as determined by Task force members (n=23) for the *Movement of substances* core concept.

Table 1: **Core concept themes and sub-themes**

1.	Substances can be in gas, liquid (dissolved or colloid), or solid form.
2.	The movement of substances within the body involves physical principles.
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4.1	Passive movement involves substances moving down a concentration or pressure gradient, governed by the physical principles driving equilibrium.
4.2.1	Active movement requires energy to move substances: Up a concentration or pressure gradient.
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4.3	For electrically charged substances, the electrical gradient must also be considered, with similar charges repelling, and opposite charges attracting.
5.	Multiple gradients can act on a substance simultaneously.
5.1	The sum of the gradients is the net force driving movement of the substance.
6.	To move within or between compartments, substances must move against various levels and forms of resistance.
6.1	Resistance can be physical or electrical.
6.1.1	Charged or polar substances cannot easily move through non-polar membranes.
6.1.2	Other characteristics, such as size of the substance also affect its movement.
6.1.3	Permeability is a measure of how easily a substance moves through a barrier. Barrier permeability affects the rate of transport.
6.1.4	Substances moving within a fluid experience physical resistance.
6.1.5	Fluid moving through a compartment experiences physical resistance.
7.	The rate of substance movement is determined by the forces acting on the substance and the resistance to movement (along with other physical principles such as temperature).
8.1	Transcellular: between compartments either side of a membrane, moving through cells.
8.2	Transmembrane: between the cellular and extracellular compartments.
8.3	Paracellular: between compartments either side of a membrane, moving around cells.
8.4	Luminal: movement within the same compartment.
9.	Transcellular transport can involve the movement of solutes through membrane-bound protein channels, pores or carriers, and pumps. These transport mechanisms can involve simple or facilitated diffusion or secondary active transport.
9.1	The transport of substances is also influenced by proteins (e.g. enzymes/protein carriers within blood).
10.	Substance transport also includes a number of forms of bulk transport.
10.1	Vesicular transport across a membrane (e.g. Endocytosis, exocytosis,

	phagocytosis...).
10.2	Movement of fluid, gas or solids along a compartment (e.g. peristalsis, ventilation).
10.3	Cell-guided flow (e.g. cilia, flagella).
10.4	Secretions (exocrine, endocrine, fluid).

Table 2: Revised themes and sub-themes incorporating reviewer feedback.

Revised Core concept themes and sub-themes
1. Substances can be in gas, liquid (dissolved or colloid), or solid form.
2. The movement of substances within the body involves physical principles.
3. Substances move through the body, either within the same compartment, or between different compartments.
3.1 Compartments can be extracellular or intracellular.
3.1.1 Movement between the intracellular and extracellular environment is referred to as Transmembrane movement.
3.1.2 Movement between extracellular compartments, which involves transmembrane movement, is referred to as Transcellular movement.
3.1.3 Movement between extracellular compartments, which *does not* involve transmembrane movement, is referred to as Paracellular movement.
3.1.4 Movement within a compartment is referred to as Luminal movement.
3.2 Compartments vary in shape and size.
3.3 Compartments can be fluid or gas filled.
4. The movement of substances can be an active or a passive process.
4.1 Passive movement involves substances moving down a concentration or pressure gradient, governed by the physical principles driving equilibrium.
4.2 Active movement requires energy to move substances up a concentration or pressure gradient, or against a resistance.
4.3 For electrically charged substances, the electrical gradient must also be considered, with similar charges repelling, and opposite charges attracting.
5. Multiple gradients can act on a substance simultaneously. The sum of the gradients is the net force driving movement of the substance.
6. To move within or between compartments, substances must move against various levels of physical or electrical resistance.
6.1 Charged or polar substances cannot easily move through non-polar membranes, which act as a barrier.
6.2 Other characteristics, such as size of the substance, and temperature of the environment also affect its movement.
6.3 Permeability is a measure of how easily a substance moves through a barrier. Barrier permeability affects the rate of movement.
6.4 Substances moving within a fluid experience physical resistance.
6.5 Fluid moving through a compartment experiences physical resistance.
7. Transmembrane or luminal transport of substances is also influenced by proteins (e.g. enzymes/protein carriers within blood).

8. Substance movement in the body can involve complex physiological transport processes such as endocytosis, exocytosis, receptor-substrate movement, phagocytosis, peristalsis, ventilation, cilia or flagella movement, etc…), which cannot be easily understood based on physical principles alone.

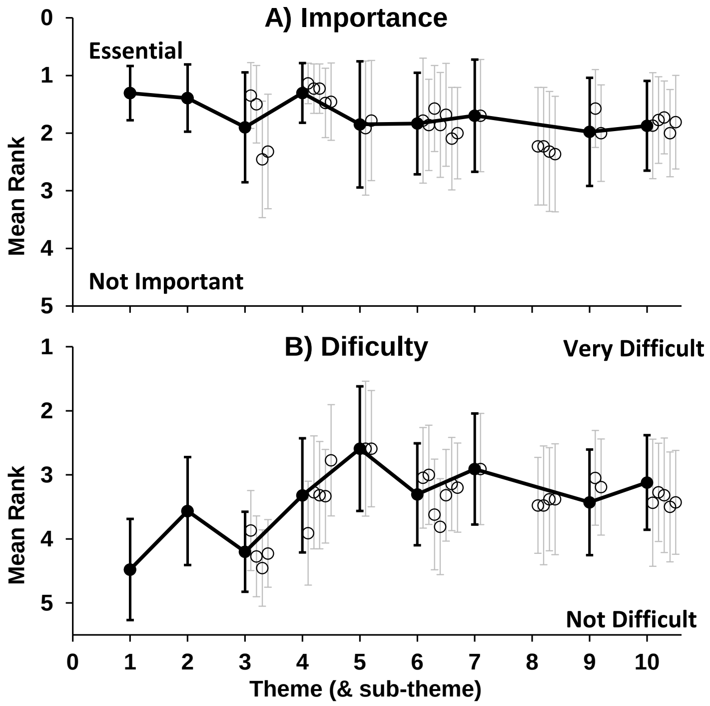

Figure 1. A) The Mean (+/-StDev) rating of importance of the major themes (solid black circles) and sub-theme (empty circles) as rated by Task force members (n=23) for *Movement of Substances* core concept. B) The Mean (+/-StDev) rating of difficulty of the major themes (solid black circles) and sub-theme (empty circles) as rated by Task force members (n=23) for *Movement of Substances* core concept. *Theme 8.0 did not incur a rating as this was introduced as a theme after the peer-review process due to feedback from reviewers.*

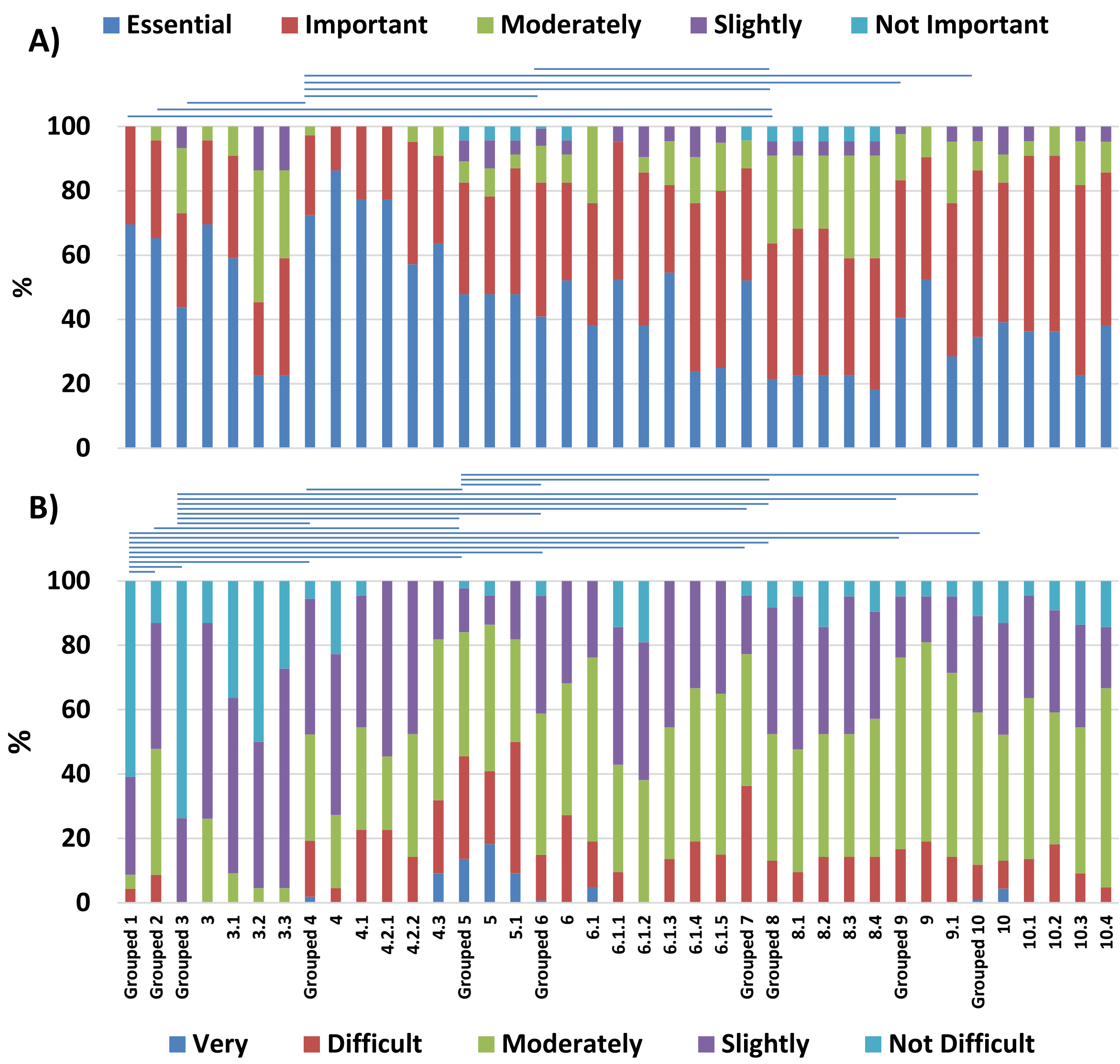

Figure 2. A): The percent ratings of importance of the major themes, sub-themes, and 'grouped' themes as determined by Task force members (n=23) for the *Movement of substances* core concept. Significant differences between the grouped themes are shown above each plot. B) The percent ratings of difficulty of the major themes, sub-themes, and 'grouped' themes as determined by Task force members (n=23) for the *Movement of substances* core concept.