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Special Section: Foundational Concepts and Assessment Tools for Biochemistry and Molecular Biology Educators, Part 1: Essential Concepts and Skills

Foundational Concepts and Underlying Theories for Majors in “Biochemistry and Molecular Biology”

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Abstract

Over the past two years, through an NSF RCN UBE grant, the ASBMB has held regional workshops for faculty members and science educators from around the country that focused on identifying: 1) core principles of biochemistry and molecular biology, 2) essential concepts and underlying theories from physics, chemistry, and mathematics, and 3) foundational skills that undergraduate majors in biochemistry and molecular biology must understand to complete their major coursework. Using information gained from these workshops, as well as from the ASBMB accreditation working group and the NSF Vision and Change report, the Core

Concepts working group has developed a consensus list of learning outcomes and objectives based on five foundational concepts (evolution, matter and energy transformation, homeostasis, information flow, and macromolecular structure and function) that represent the expected conceptual knowledge base for undergraduate degrees in biochemistry and molecular biology. This consensus will aid biochemistry and molecular biology educators in the development of assessment tools for the new ASBMB recommended curriculum. © 2013 by The International Union of Biochemistry and Molecular Biology, 41(5):289–296, 2013

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Introduction

Biochemistry and molecular biology is increasingly recognized as a unified discipline, rather than as two separate and distinct disciplines or subdisciplines—biochemistry, centered in chemistry, and molecular biology, centered in biology. Recognizing this, the American Society for Bio-

chemistry and Molecular Biology (ASBMB) developed a suggested curriculum, which was published in 2002 [1]. Since then several reports, including the “Vision and Change” [2] and “PCAST,” [3] reports have suggested that undergraduate education in life sciences should be focused on broad conceptual understanding of the “Big Ideas” (In this article we use the term “Foundational Concepts”) of the discipline rather than detailed knowledge of discipline specific content. Modern molecular life science is increasingly interdisciplinary [4] and many advances of the future will be made at the interface between the disciplines emphasizing the importance of understanding how these broad disciplinary concepts relate to other disciplines, such as chemistry and physics, and on the necessary skills needed to pursue a career in science.

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To move education of our students from the more traditional content based education to this new vision of undergraduate education requires broad agreement on what the disciplinary foundational concepts are and on how to assess conceptual understanding rather than the more traditional specific fact based knowledge. To address these challenges ASBMB applied for, and was awarded, an RCN-UBE grant from the National Science Foundation (Award number 0957205 "RCN-UBE: "Promoting Concept Driven Teaching Strategies in Biochemistry and Molecular Biology through Concept Assessments," Ellis Bell, PI). A crucial step in this process is the development of a consensus of what the foundational conceptual areas of biochemistry and molecular biology are. The working group for the "Biochemistry and Molecular Biology (BMB) Foundational Concepts" has developed such a list through discussion at and feedback from a series of regional workshop meetings involving several hundred educators from a wide variety of institutions including major research universities, liberal arts colleges, and minority serving institutions, and well-attended sessions at the last two Annual Experimental Biology National Meetings in 2012 and 2013, and the ASBMB sponsored Student Centered Education in the Molecular Life Sciences Meeting, held in Richmond, VA in 2011.

The purpose of this article is to introduce a group of foundational concepts; broad, conceptual topics that most educators agree are seminal to the education of any biochemistry and molecular biology major. In addition, to illustrate the alignment of these foundational concepts to learning objectives we have developed a short list of sample learning outcomes and objectives based on each conceptual area to both further clarify each one and to act as a stimulus for the development of more course-specific learning objectives by faculty. As the project further progresses, teaching resources (sample course curricula, teaching materials, and assessment instruments focusing on these conceptual areas) will be deposited in an online resource and should facilitate the future development of assessment tools by both individuals and organizations.

There are numerous ways to think about the design of a curriculum, course, or lesson. One general way to examine this process is to outline what we want students to learn, how we plan to deliver that knowledge, how we want to assess that the students have learned the material, and how we plan to perform subsequent iterations to fill in gaps in knowledge. This is an assessment cycle. Whether conscious of this assessment cycle or not, we often perform it in any course and incorporate it in curricular design. Fundamental to this process is an understanding of what the expectations are for the student. There need to be clear expectations determined at the outset for what the student should know at the end of each lecture, unit, or course. Without these there can be no clear path for either students or educators to follow, and assessment of learning becomes at best murky.

The Need

First, as educators we are increasingly being held responsible for what we teach, both inside our own institutions and from outside bodies. Biochemistry and molecular biology programs are a diverse group with some heavily grounded in chemistry while others have more of a biological foundation. Expectations differ from campus to campus and accrediting body to accrediting body. Before we can begin to assess what students know, there needs to be general consensus as to what we expect from them. Furthermore, as biochemistry and molecular biology are complex and constantly evolving topics, a taxonomy of concepts and skills will be useful to anyone attempting assessment or developing new assessment tools. This consensus list of foundational concepts attempts to organize and provide examples in a distilled and streamlined manner to facilitate the development of new assessment methods in line with the new ASBMB undergraduate degree accreditation program.

Second, we need some measure that we are teaching material that is current, pertinent, and useful to our students. It does our students no good if we are supplying them with course content that prepares them for careers of the past. A consensus list of foundational concepts is one way that we can begin to outline and organize what our students know. From that, other pieces of the educational puzzle (e.g., how we assess what they know and how we helped deliver and build that knowledge) begin to fall into place. Third, we currently lack the ability to compare between programs in any sort of quantitative manner. It would be useful to have a simple metric to provide to graduate programs or companies to demonstrate that our students are well prepared and can meet the challenges set out for them. Finally, we feel strongly that biochemical educators should be the ones driving this change, instead of waiting for other outside groups to prescribe to us what our courses and majors should contain.

We need simple, accurate means of assessment that parallel our classroom and laboratory practices and indicate where we are and where we are not making the mark. However, before we do this we must recognize that defining concepts is necessary before any attempts are made to develop assessment tools. We must first define what we want to assess before we decide how to assess it.

Our Solution

This project seeks to define the core concepts of biochemistry and molecular biology. These are the most fundamental underpinnings of the field that all undergraduate biochemistry and molecular biology majors should be equipped with when they graduate.

We have assembled a list of five broader core concepts common to all of biochemistry and molecular biology. These are evolution, matter and energy transformation, homeostasis, biological information, and macromolecular structure and

function. The concepts we chose were based on the Vision and Change NSF report, the core concepts learning objectives list from the ASBMB accreditation report, the input of faculty members from around the country at regional meetings, and our personal experiences. The list is not meant to be proscriptive or limiting, but is rather meant to categorize and define concepts and individual topics for pedagogical purposes.

From these core concepts we developed a list of four or five recurring themes for each concept (memes if you will) that can be found repeated throughout all of biochemistry. These illustrate, broaden, and define the concept in a somewhat more detailed fashion but are still lacking in terms of a specific example. Finally, we developed a list of more detailed statements that related to the themes and concepts. These statements are more detailed but still general enough to allow significant leeway for future groups or individual faculty members to develop more specific learning objectives and assessment tools.

About the Learning Outcomes

Associated with each of the core concepts we have provided sample learning outcomes (or learning objectives). These are representative and are meant to be used as examples to help educators develop their own outcomes and assessment tools. The outcomes have a common structure (“Students should be able to...”) and contain two or three verbs chosen from Bloom’s taxonomy [5]. These outcomes were developed so that each one had one lower level Bloom’s verb that focused on basal knowledge (e.g. describe) and several others that focused on higher levels of cognition (e.g. analyze, relate, design, and discuss). These verbs are found in bold in the learning outcome. Although the need to establish learning outcomes and assessments that strengthen students’ grasp of the foundational knowledge (unifying concepts) of biochemistry and molecular biology is clearly understood, we as college level educators and scientists also appreciate the need to include aspects of data interpretation and experimental design as well as the essential allied fields in these learning outcomes and assessments, something that will be more explicitly addressed in future refinements of this project and are the subject of the accompanying papers [6, 7].

The Core Concepts and Sample Learning Outcomes (Presented Without Any Specific Order Implied)

Evolution

The Central Importance of the Theory of Evolution to All Biological Sciences

As it is for all biological sciences, evolution is a foundational concept in biochemistry and molecular biology. An understanding of the shared evolutionary history of all liv-

ing systems on our planet is thus critical for any student of these disciplines. Evolutionary theory guides experimental efforts across biochemistry and molecular biology. This ranges from the comparison of related enzymes from different species by the identification of key active site residues to the use of interspecies comparisons in the determination of gene functions to the search for genes responsible for genetic diseases using phylogenetic approaches to the study of the regulatory mechanisms that guide development. Our attempts to understand human molecules and processes are enhanced immeasurably by our understanding of their counterparts in other organisms. Our efforts to address a new human pathogen–viral, bacterial, or eukaryotic–are enhanced immeasurably by previous studies of viruses or organisms related to the pathogen.

Students should be able to describe examples of evolution to a lay audience, value the principles of evolution through natural selection as foundational to biochemistry and molecular biology, and defend these principles in their work, schools, and communities.

The Basics of Darwin’s Theory of Evolution

The earth is ~4.6 billion years old. All known life on the planet has descended from a common ancestor that existed over 3.5 billion years ago. Differentiation into the myriad of extant species has occurred by a process of slow evolution driven by natural selection.

The Process of Natural Selection

Slight, random, heritable changes (mutations) produce diversity in a population. Alterations may decrease, increase, or have no effect on fitness in a particular environment. Deleterious mutations are more common than advantageous ones. Those alterations that increase fitness give some members of a population a survival advantage. Adapted individuals are more likely to reproduce, and thus, are more likely to contribute genetically to the next generation. Over generations, this process gradually leads to an increase in fitness for the population in that given environment. Natural selection is manifested at all levels of biology including ecosystems, speciation, population dynamics, physiology, cell biology, and molecular biology.

Students should be able to use the tools of biochemistry and molecular biology (including databases of biological molecules and functional assays) to explain changes in traits, adaptations, and the success or failure of organisms and species.

Evidence for the Theory of Evolution

The theory of evolution is broadly supported by an internally consistent and intersupporting array of millions of studies that have accumulated over the past 150 years (since Darwin). The studies come from biochemistry, genetics, molecular biology, modern genomics, astronomy, geology, paleontology, prebiotic chemistry, the macroecology of islands, developmental biology, and many other disciplines.



The shared history of organisms on this planet is evident in their common genetic code, metabolic pathways, chemical approaches to catalysis, and processes of information transfer. Evolution is directly observed in the laboratory in long-term evolution trials with microorganisms, in medicine as pathogens adapt to common therapies, and in agriculture, as plants and pests adapt to human efforts at control. Evolution is not just a set of unifying principles; it is an ongoing process and challenge affecting human health and prosperity.

Students should be able to analyze pre-existing or novel data and relate the findings in light of the theory of evolution.

The Molecular Basis of Natural Selection

Selection is driven by challenges inherent to an environment. The heritable genotypes of different individuals of the species change over time through random, heritable changes (alteration of the sequence of nucleotides; mutations) in an organism's germ line DNA, or germ line RNA in some cases (e.g. RNA viruses) and arise during DNA replication or via unrepaired DNA damage. These contribute to population diversity. At the molecular level, evolution and natural selection are manifested in terms of altered gene expression or gene product function resulting from these physical alterations in the heritable genetic information. Acquisition of new traits or structures is facilitated by gene duplication, wherein one copy of a gene can evolve to acquire a new function. Diversity in a population renders individuals in that population more or less fit in a given environment. Genetic alterations that improve fitness tend to increase in frequency within a population in succeeding generations.

Students should be able to describe what a mutation is at the molecular level, and how it comes about, be able to predict how changes in a nucleotide sequence can influence the expression of a gene or the amino acid sequence of the gene product (protein) and be able to translate these findings into a conclusion about how said mutation would impact the general fitness of an organism or population.

Matter and Energy Transformation

The Many Forms of Energy Involved in Biological Processes

The energetics of a biological system or process—be it an ecosystem, an organism, a cell, a biochemical reaction—conforms to and is understood in terms of the fundamental laws of thermodynamics. Biological systems capture and process energy from the environment in many forms including that emanating directly from the sun (photons through photosynthesis), heat from the environment (kinetic energy), and energy rich compounds produced by geothermal processes (e.g. sulfur compounds) or other organisms (e.g. carbohydrates). Energy from all sources is

chemically converted into useful chemical and physical work in a controlled and regulated fashion. The potential energy stored in chemical bonds can be used to generate motion, light, heat, and electrochemical gradients; likewise, electrochemical gradients can be used to generate motion and new chemical bonds. The input of energy from the environment allows living systems to exist in a state of nonequilibrium with their environment. The discussion of energy and matter conversions in biological systems makes use of the physical concept of changes in Gibbs free energy, or ΔG .

Catalysis

Biologically relevant energy and matter interconversions do not occur rapidly enough (often by many orders of magnitude) to support life. In living systems, biological catalysts called enzymes facilitate these reactions. Enzymes are macromolecules, usually proteins or RNA molecules with a catalytic function. Enzymes do not alter reaction equilibria; instead, they lower the activation barrier of a particular reaction so that reactions proceed much more rapidly. The presence of powerful enzymatic catalysts is one of the key conditions for life itself.

Description of the rates of enzymatic reactions represents the subdiscipline enzyme kinetics. Key concepts of kinetics, including the definitions of the terms v_0 , V_{max} , K_m , and k_{cat} , constitute a common language for biochemists and molecular biologists in discussing the properties of enzymes.

Students should be able to apply their knowledge of basic chemical thermodynamics to biologically catalyzed systems, quantitatively model how these reactions occur, and calculate kinetic parameters from experimental data.

Coupling Exergonic and Endergonic Processes

Biochemical systems couple energetically unfavorable reactions with energetically favorable reactions to allow for a wider variety of reactions to proceed.

Students should be able to discuss the concept of Gibbs free energy, and how to apply it to chemical transformations, be able to identify which steps of metabolic pathways are exergonic and which are endergonic and relate the energetics of the reactions to each other.

The Nature of Biological Energy

In biological systems, chemical energy is stored in molecules with high group transfer potential or strongly negative free energy of hydrolysis or decomposition. These molecules, particularly ATP, provide the free energy to drive otherwise unfavorable biochemical reactions or processes in tightly coupled and highly controlled fashion. Most frequently, the free energy needed for a process or metabolic pathway is provided by group transfer rather than by hydrolysis. In this way, efficient energy transfer is optimized, while inefficient energy transfer to the environment (in the form of heat for example) is minimized.

Students should be able to show how reactions that proceed with large negative changes in free energy can be used to render other biochemical processes more favorable.

Homeostasis

Biological Needs for Homeostasis

Biological systems operate under a relatively narrow and controlled set of conditions; as such, there is a need to maintain rigorous control over the concentrations of metabolites and small molecules in the cell. The cell is the basic physical unit of all organisms in that it creates a homeostatically controlled environment for rigorously maintaining the balance of energetically favorable and unfavorable chemical and physical processes within the confines of the cell as required for sustaining the life of the cell.

Linked Steady State Processes and Homeostasis

Homeostasis is ultimately dictated by two laws of the thermodynamics: 1) Exergonic processes in the homeostatic environment of the cell must lead to a net loss in Gibbs free energy ($\Delta G < 0$). Any favorable reaction must expend the capacity to do chemical work, as quantified by the Gibbs free energy. 2) Any exergonic reaction or process must ultimately lead to an increase in entropy or net “disorder” of the universe ($\Delta S > 0$). Biological homeostasis is largely maintained by systems of irreversible nonequilibrium steady-state reactions, although rapid equilibrium reactions (such as occur with cell buffers, including pH buffers and oxygen buffers like Hb and Mb) contribute to homeostasis. While all biochemical reactions are “reversible” (some more so than others on a temporal scale) and tend toward equilibrium, the overall chemical system in a cell is maintained in a state with nonequilibrium steady state concentrations of reactants and products.

Students should be able to relate the laws of thermodynamics to homeostasis and explain how the cell or organism maintains homeostasis (a system seemingly in equilibrium) using nonequilibrium mechanisms.

Quantifying Homeostasis

The tendency of chemical reactions and processes to occur under homeostatic conditions in the cell is understood and quantifiable with the equation for the change in Gibbs free energy, ΔG , as based on the steady concentrations, not the equilibrium concentrations, of reactants and products. Because ΔG is a measure of amount of chemical work a process can yield, $\Delta G < 0$ for any process that would tend to produce products in the presence of a suitable catalyst. Biological systems have evolved to harness chemical work from hundreds of reactions that occur in the cell in any given time period.

Organization of Chemical Processes

Reactions critical to living systems are organized into pathways by which key cellular metabolites are interconverted.

Organization into pathways facilitates regulation required for the maintenance of homeostasis. Pathways or parts of pathways are often organized structurally as well as chemically, with pathway enzymes linked or sequestered in some manner. Pathways are sometimes separated from each other by structural compartments within cells.

Control Mechanisms

Homeostasis within a cell or organism is regulated in many ways, for example by alterations in gene expression, covalent modifications of proteins catalyzing key steps in a pathway, allosteric regulators, the action of regulatory proteins and RNA molecules, and activation or inactivation of enzymatic catalysts by proteolytic or nucleolytic cleavage.

Students should be able to summarize the different levels of control (including reaction compartmentalization, gene expression, covalent modification of key enzymes, allosteric regulation of key enzymes, substrate availability, and proteolytic cleavage), and relate these different levels of control to homeostasis

Cellular and Organismal Homeostasis

Homeostasis in the cell is maintained by regulation, and by the more or less steady state exchange of materials and energy with its surroundings (e.g. taking in nutrients, expelling metabolic byproducts, releasing heat into the surroundings). All of these processes occur if the appropriate catalyst is present and if the net entropy of the universe increases as a result of the process ($\Delta S > 0$), and there is an accompanying net loss of free energy ($\Delta G < 0$).

Homeostasis in an organism or colony of single celled organisms is regulated by secreted proteins and small molecules, often functioning as signals. Each chemical signal in an organism is transiently bound by specific macromolecular receptors (usually proteins), leading to an alteration in conformation, interactions with other components of one or more signaling pathways, and changes in downstream metabolic processes.

Students should be able to describe homeostasis at the level of the cell, organism, or system of organisms and hypothesize how the system would react to deviations from homeostasis.

Biological Information

The Genome

Two key conditions for life include the presence of powerful biological catalysts, and heritable information to guide the production of those catalysts. The information for an organism’s enzymatic catalysts, as well as for proteins and RNA molecules with structural, transport, signaling, and ligand-binding functions, is stored in its genome. The genome is comprised of linear polymers of four nucleotides, called nucleic acids, assembled into unique sequences that encode the information needed to specify the macromolecules particular to that organism. An organism’s genome is



usually encoded in double-stranded deoxyribonucleic acid (dsDNA) polymers but the genomes of some microbes are comprised of single-stranded or double-stranded ribonucleic acid (ssRNA or dsRNA) polymers. The dsDNA polymers may be very long and encompass millions of nucleotides in each strand. Complete polymers are called chromosomes. The nucleotides of one strand of a DNA chromosome form complementary base pairs with the nucleotides of the other strand, with adenosine residues paired with thymidine, and guanosine paired with cytidine.

Hereditary information passed on from one generation of a species to the next may include all of the genome of the organism (asexual reproduction) or a portion of the genome (sexual reproduction). The heredity of multicellular organisms also depends on the transmission of mitochondrial or chloroplast dsDNA from parent to offspring. The transmission of epigenetic imprinting from one individual to the next is also important.

Students should be able to define what a genome consists of, and how the information in the various genes and other sequence classes within each genome are used to store and express genetic information.

Information in the Gene: Nucleotide Sequence to Biological Function

The unit of genetic information in a nucleic acid that specifies some macromolecular product (protein or RNA) is called the gene. The information in a gene is converted into single-stranded RNA in a process called transcription. Those RNAs derived from protein-encoding genes (called “messenger RNA” or mRNA), are then “translated” by ribosomes into protein molecules. Proteins consist of linear sequences of amino acid residues whose order is determined by the sequence of mRNA nucleotides, utilizing a universal genetic code (minor exceptions to code universality are readily explained by evolutionary theory).

All known organisms—bacteria, archaean, or eukaryote—utilize the same pool of 20 “standard” amino acids for protein synthesis, the same genetic code to translate mRNAs and guide that synthesis, and the same set of four nucleotides to constitute genomic nucleic acids.

Students should be able to explain the central dogma of biology (the message in DNA is transcribed into RNA and translated into protein) and relate the commonality of the process to all of life.

Genome Transmission from One Generation to the Next

Passing a copy of the genome to a new cellular generation requires genome duplication, a process called replication. Each strand of the double-stranded DNA comprising a chromosome is used to direct the synthesis of a complementary strand, leading to the generation of two identical dsDNA products. One copy of the replicated genome is passed to the daughter cell when the cell divides.

Students should be able to illustrate how DNA is replicated and genes are transmitted from one generation to the next in multiple types of organisms including bacteria, eukaryotes, viruses, and retroviruses.

Genome Maintenance

Because genetic mutations can be quite deleterious to an organism and/or its progeny, there is a low biological tolerance for genomic alterations. For this reason, the nucleic acids in chromosomes are nearly unique in that they are the objects of elaborate and energy-intensive repair processes. Repair affords a high degree of genomic stability in most organisms, and limits the rate of evolutionary processes. In higher eukaryotes, including mammals, defects in DNA repair processes produce genomic instability and can lead to cancer.

Students should be able to state how the cell insures high fidelity DNA replication and identify instances where the cell employs mechanisms for damage repair.

Macromolecular Structure and Function

Biological Macromolecules are Large and Complex

Macromolecules are polymers of basic molecular subunits. They include the proteins (made up of amino acids), nucleic acids (comprised of nucleotides), carbohydrates (polymers of sugars), and lipids (with a variety of hydrophobic molecular constituents). The understanding of protein and nucleic acid structures is the most advanced. The functions of macromolecules include catalysis (protein and RNA enzymes), ligand-binding, cellular structure, signaling, and transport. Macromolecules can be very large. Nucleic acids in chromosomes have molecular weights ranging into the billions. Proteins (single polypeptide chains) range in size up to molecular weights of a million or more.

Students should be able to discuss the diversity and complexity of various biologically relevant macromolecules and macromolecular assemblies in terms of the basic repeating units of the polymer and the types of linkages between them

Structure is Determined by Several Factors

Under a given set of conditions, most macromolecules tend to fold into one or a few semistable three-dimensional conformations. The structure of macromolecules is dictated by the sequence of amino acids (linked by peptide bonds), nucleotides (linked by phosphate diester bonds), or other constituents in the polymer, other covalent bonds linking the polymeric constituents, the pattern of weak noncovalent interactions between chemical groups within the folded structure, and the noncovalent and thermodynamic interactions between chemical groups of the structure and compounds present in its immediate environment.

Weak, noncovalent interactions—the hydrophobic effect, hydrogen bonds, ionic interactions, Van der Waal's interactions—play a special role in the folding of a large polymeric macromolecule into a particular active conformation. The hydrophobic effect makes the largest contribution to the structural stability of proteins and nucleic acids that are soluble in aqueous environments.

Portions of a macromolecule may fold up into a semi-stable conformation independently of other segments of the same macromolecule. These independently stable segments are called domains.

Students should be able to discuss the chemical and physical relationships between sequence and structure of macromolecules and evaluate chemical and energetic contributions to the appropriate levels of structure of the macromolecule and predict the effects of specific alterations of structure on the dynamic properties of the molecule.

Structure and Function are Related

The function of a protein, nucleic acid, or other macromolecule is defined to a large extent by the specific molecular interactions it takes part in. Those interactions are in turn dictated by the structure of the macromolecule. If a protein or nucleic acid has a ligand-binding function, it will have a depression in its surface (a binding site) that is complementary in size, shape, charge, and other features to the ligand molecule to which it binds. If the protein or nucleic acid has a catalytic function, it will similarly have a depression on its surface (an active site) structured to facilitate catalysis of a particular reaction. If a protein or nucleic acid has a structural function, it will have a structure that confers strength or elasticity or whatever is required for a particular structural role in a cell or organism.

Students should be able to examine a structure of a macromolecule-ligand complex and predict the determinants of specificity and affinity and design experiments to test their hypothesis, explaining the basis of the proposed experiments and discussing potential results in the context of the hypothesis.

Macromolecular Interactions

The interactions between macromolecules and other molecules rely on the same weak, noncovalent interactions that play the major role in stabilizing the three-dimensional structures of the macromolecules themselves. The hydrophobic effect, ionic interactions, and hydrogen bonding interactions are prominent. The structural organization of interacting chemical groups in a binding site or an active site lends a high degree of specificity to these interactions.

Macromolecular Structures are Dynamic

Macromolecular structures are not static. Conformational changes large and small are often critical to function. Small changes can come in the form of localized molecular vibrations that can facilitate the access of small molecules to interior portions of the macromolecule. Large conforma-

tional changes can come in the form of the motions of different macromolecular domains relative to each other to facilitate catalysis or other forms of work.

Some Macromolecules are Intrinsically Unstructured

Segments of some proteins, and in a few cases entire proteins, are intrinsically unstructured. The unstructured segments often take up a particular three-dimensional structure when they interact with another macromolecule. The lack of structure in solution may facilitate a function in which interactions must occur promiscuously with several other molecules, as documented for some proteins with a signaling function.

Macromolecular Function is Subject to Regulation

Following completion of polypeptide synthesis by the ribosome (post-translation), nascent polypeptides are almost invariably covalently modified in some functionally important way before, during, and/or after folding into their three-dimensional conformations. A wide variety of possible covalent modifications (e.g. partial proteolytic cleavage, intrachain and/or interchain disulfide formation, glycosylation, and phosphorylation) occur, and play a role in regulation, cellular targeting of the protein, or directly in the protein's function. Nucleic acids also undergo a variety of modifications that affect their function, including the modification of bases in RNAs, and the methylation of some cytosine residues in eukaryotic DNA.

Students should be able to compare and contrast the potential ways in which the function of a macromolecule might be affected and be able to discuss examples of allosteric regulation, covalent regulation, and gene level alterations of macromolecular structure/function.

Each of these broad learning goals can be unpacked to give more specific, course related learning goals that can then be used to form the basis of specific assessments of student understanding in the context of the appropriate conceptual area.

Benefits of this Solution

We believe there are several benefits to adopting these core concepts and using them in the future development of assessment tools. First, the concepts are broad. It is hard to envision a topic that is fundamental to undergraduate biochemistry education that is not covered by at least one of the concepts. Second, using recurring themes and detailed statements we have attempted to provide guidance for educators and more clearly define the core concept. These themes and statements have also been defined broadly enough to allow flexibility for the development of learning objectives and assessment tools.

Our hope is that these foundational concepts will be beneficial to biochemical educators in that they will be



broad enough and flexible enough to guide future curricular changes while still providing structure.

Resources Used in the Development of the Foundational Concepts

These concepts should resonate and sound familiar. The BMB Foundational Concepts working group of the RCN-UBE group has developed this list based on the 2010 NSF-AAAS Vision and Change report [2], former ASBMB curricular guidelines [1], the ASBMB Policies and Procedures for Accrediting Bachelor's Degrees in Biochemistry and Molecular Biology report [8], and the input of hundreds of educators who attended regional ASBMB meetings held over the past two years.

This inventory is not intended to be static and should evolve over time as biochemistry and molecular biology continue to change and new technologies become available. We also hope that this list is not proscriptive, but rather informs individual educators and groups who are developing new assessment tools. Finally, while we recognize that the development of assessment tools and methods are not part of this project, we hope that this inventory facilitates the exchange of ideas and tools for developing more complex types of assessments.

Future Objectives

Over the first two years of this project the RCN sought to build a network of educators and foster a broader understanding of the issues pertinent to all in terms of content and assessment. In the third year we are focused on facilitating the exchange of ideas and tools for developing more complex types of assessment. It is this working group's hope that the list of core concepts, themes, and applications will be both flexible enough to accommodate a wide range of views and concrete enough to facilitate the development of tools to directly assess students comprehension and ability to apply these concepts.

The ultimate goal of this project is the creation of an ongoing web based resource for biochemical educators that will help provide them with the resources and methods to develop assessment tools though not provide those tools themselves. By building networks of educators, we aim to

promote and make more efficient the development of tools for the assessment of foundational concepts. Our hope is that resource will continue to grow and evolve with changes in the field, while still serving fundamental needs.

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