Chapter 4

Skills and Foundational Concepts for Biochemistry Students

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This chapter is intended for faculty and prospective faculty teaching biochemistry and molecular biology (or related molecular life science) courses, and for biochemistry and molecular biology program directors or departmental chairs responsible for the planning of and/or implementing appropriate degree programs. The chapter reviews the evolution of curricular suggestions for biochemistry and molecular biology majors from the turn of the millenium to the present day. The major driving force for curricula change has been the Vision and Change report that continued an emphasis on concepts and skills rather than simply content. From the perspective of Vision and Change, we discuss and compare curricular recommendations from the American Chemical Society and the American Society for Biochemistry and Molecular Biology, and compare them to recommendations for pre-medical school students taking biochemistry courses. We discuss some of the concept areas and skills, and emphasize student-centered teaching approaches and high impact teaching practices in the context of education in biochemistry and molecular biology. We illustrate several of these areas in sufficient detail, with scoring rubrics, to indicate appropriate levels of student performance, and discuss the ASBMB certification exam. The chapter concludes with a discussion of what an idealized curriculum should look like to best serve its students, including a brief discussion of the importance of inclusive teaching.

Introduction: Concepts Conquer Content

In order to discuss current curricular recommendations of the major professional societies it is important to analyze how these have evolved. As early as 1986, with the undergraduate science mathematics and engineering education report from the national science board (*1*), there were calls to improve biology education at the college level. In 2001, an article in Nature Reviews, "The Future of Education in the Molecular Life Sciences" (*2*) called for increased student-centered education with more focus on skills and concepts and the central role that undergraduate research can play. Discussion continued with the 2003 publication of "Bio 2010 transforming undergraduate education

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for future research biologists" (*3*) and other publications (*4*, *5*). This coincided with the Education and Professional Development committee of the American Society for Biochemistry and Molecular Biology releasing a revised recommended curriculum (*6*), Tables 1 and 2.

How these recommendations might be put into effect in various types of Colleges and Universities was illustrated by a series of articles in Biochemistry and Molecular Biology Education (*7–9*). These revisions signaled the start of a move from content to concepts and skills, and, instead of listing required courses, described concept and content areas and skills that should be developed across a biochemistry and molecular biology degree curriculum.

Vision and Change: Curriculum Not Courses

Recognizing not only the changing nature of the biological sciences (*2*) but also the changing demographics of the nation, exacerbated by continued low retention in the sciences of students from underrepresented groups and projections for increased needs of a science literate workforce, the National Science Foundation,in 2006, in conjunction with AAAS, the National Institutes of Health and the Howard Hughes Medical Institute initiated what was to become known as "Vision and Change". To achieve maximum buy-in from institutions and faculty, the final report of the Vision and Change initiative, "Vision and Change in Undergraduate Biology Education: A Call to Action (*10*)" resulted from national conversations involving hundreds of educators, faculty, administrators and students as well as the major funding agencies.

Vision and Change continued the emerging trend of focusing on conceptual areas and skills and categorized these as shown in Figure 1 and Table 3.

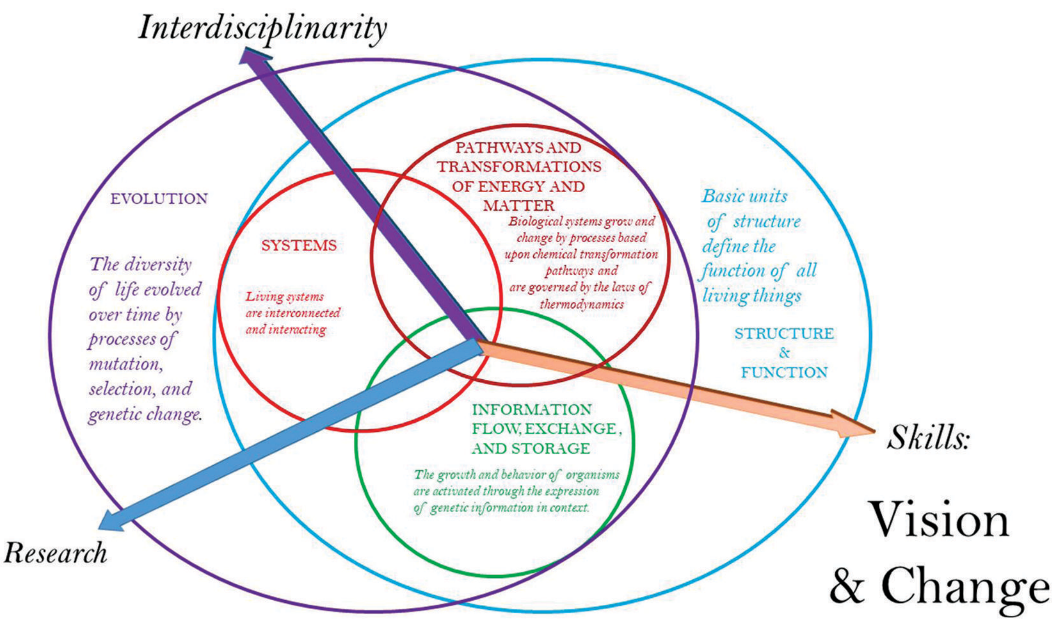

Figure 1. Key features of the vision and change recommendations for biology education.

Table 1. 2004 Recommended Curriculum for a Biochemistry and Molecular Biology Undergraduate Major

Level	*Biochemistry and Molecular Biology*	*Chemistry Core Topics*	*Biology Core Topics*
Introductory	Introductory enzyme kinetics, allosteric regulation, Bioenergetics and equilibria, DNA/RNA structure and function.	Atomic structure, molecular structure and spectroscopy, periodicity, thermodynamics, kinetics, bonding (covalent and noncovalent), reactions and stoichiometry, acids/bases, descriptive inorganic, transition metals, redox	Cell structure, biomolecule structure and function, protein structure/function
Intermediate	enzyme kinetics, mechanisms of reversible and irreversible enzyme inhibitors, ligand binding, detailed chemical mechanisms of enzymes. Metabolism and regulation, signal transduction, supramolecular assemblies	Structure/bonding/nomenclature, functional groups, instrumental structure determination, stereochemistry, synthesis, reaction mechanisms and intermediates, molecular recognition, organometallics, combinatorial chemistry, bioorganic (amino acids, peptides, lipids, carbohydrates, nucleotides).	Concepts of compartmentation and tissue specialization, including plant, animal, bacterial, fungal cells, etc. The "Central Dogma."
Advanced	Advanced topics in protein structure and function: Advanced topics in protein structure and function: enzyme kinetics, mechanisms of reversible and irreversible enzyme inhibitors, ligand binding, detailed chemical mechanisms of enzymes, protein folding, molecular basis for protein function, regulation of protein activity, proteomics	Physical biochemistry: thermodynamics, kinetics, molecular spectroscopy, solutions and equilibria, ligand interactions, molecular modeling	Advanced discussion of classical genetics and the "Central Dogma": DNA replication, transcription and translation, topics in DNA/RNA structure/function, genomics, regulation of gene expression in prokaryotes and eukaryotes, protein synthesis and processing, genetic engineering techniques, bioinformatics.
Laboratory Skills	Isolation and characterization of proteins and other biomolecules, enzyme kinetics and inhibition,	spectroscopy (*e.g.* UV/VIS, fluorescence, NMR, MS), chromatography (HPLC, etc.), electrophoretic techniques (*e.g.* PAGE, IEF, CE, etc.).	DNA isolation and sequencing, cloning, PCR, genetic engineering techniques, microscopy, aseptic techniques, microarrays

Table 1. (Continued). 2004 Recommended Curriculum for a Biochemistry and Molecular Biology Undergraduate Major

Level	*Biochemistry and Molecular Biology*	*Chemistry Core Topics*	*Biology Core Topics*
	genetic engineering techniques, quantitative techniques, data acquisition/statistics, use of computer databases,		
Research	Experimentally-based research, including a formal proposal, report, and presentation(s)		

Table 2. Skills That Biochemistry and Molecular Biology Students Should Obtain by the Time They Have Finished Their Undergraduate Program

Science Related	Understanding of the fundamentals of chemistry and biology and the key principles of biochemistry and molecular biology. Awareness of the major issues at the forefront of the discipline. Ability to dissect a problem into its key features. Ability to design experiments and understand the limitations of what the experimental approach can and cannot tell you. Ability to interpret experimental data and identify consistent and inconsistent components. Ability to design follow-up experiments
Communication	Ability to use oral, written, and visual presentations to present their work to both a science-literate and a science-non-literate audience. Ability to assess primary papers critically. Ability to think in an integrated manner and look at problems from different perspectives. Awareness of the ethical issues in the molecular life sciences.
Quantitative	Ability to use computers as information and research tools. Good “quantitative” skills such as the ability to accurately and reproducibly prepare reagents for experiments. Awareness of the available resources and how to use them.
WorkPlace	Ability to work safely and effectively in a laboratory. Ability to collaborate with other researchers.

Table 3. Foundations of "Vision and Change"

Conceptual Areas	Evolution: Structure and function: Information flow, exchange , and storage : Pathways and transformations of energy and matter: Systems:
Skills	ABILITY TO APPLY THE PROCESS OF SCIENCE: *Biology is evidence-based and grounded in the formal practices of observation, experimentation, and hypothesis testing.* ABILITY TO USE QUANTITATIVE REASONING :*Biology relies on applications of quantitative analysis and mathematical reasoning.* ABILITY TO USE MODELING AND SIMULATION: *Biology focuses on the study of complex systems.* ABILITY TO TAP IN TO THE INTERDISCIPLINARY NATURE OF SCIENCE: *Biology is an interdisciplinary science.* ABILITY TO COMMUNICATE AND COLLABORATE WITH OTHER DISCIPLINES : *Biology is a collaborative scientific discipline.* ABILITY TO UNDERSTAND THE RELATIONSHIP BETWEEN SCIENCE AND SOCIETY: *Biology is conducted in a societal context.*

As a result of the Vision and Change initiative, the American Society of Biochemistry and Molecular Biology, using the NSF Research Coordination Network-Undergraduate Biology Education funding mechanism, convened a nationwide series of meetings over the next five years that resulted in a series of papers in Biochemistry and Molecular Biology Education, focusing on giving further definition to the concept areas that constitute biochemistry and molecular biology (Tansey et al.), the requisite skills (White et al.) and interdisciplinary concepts (Wright et al.) (7–9) which are summarized in Figure 2.

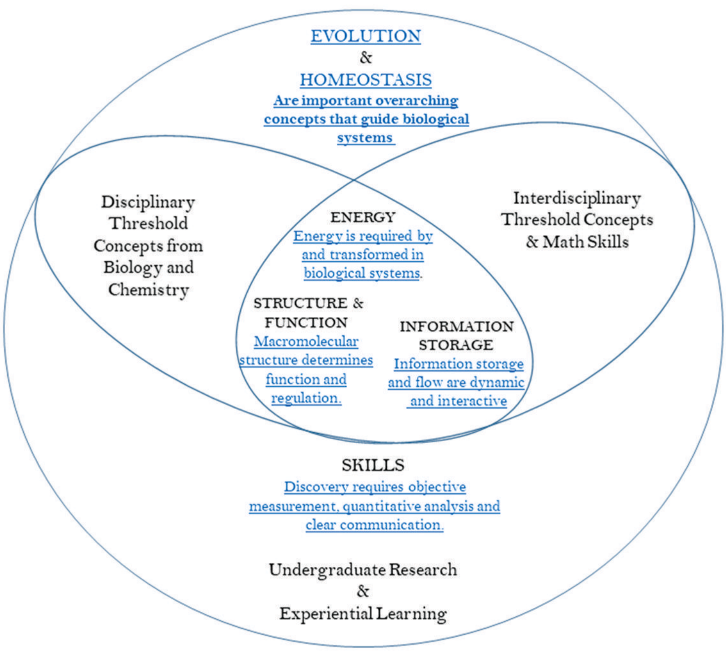

Figure 2. Summary of concepts and skills recommended by the American Society for Biochemistry and Molecular Biology.

These conceptual areas and skills became the foundation of the American Society for Biochemistry and Molecular Biology's accreditation program and exam, as well as Course Source's "Biochemistry and Molecular Biology Learning Framework" (*11*, *12*). Current curriculum recommendation from the American Society of Biochemistry and Molecular Biology's are based on these conceptual areas and skills.

For example, in the section on the Foundational Concepts of Macromolecular Structure and Function, the necessary foundational concepts are framed in the form of eight questions (learning goals):

What factors contribute to the size and complexity of biological macromolecules?

What factors determine structure?

How are structure and function related?

What is the role of noncovalent intermolecular interactions?

How is macromolecular structure dynamic?

How is the biological activity of macromolecules regulated?

How is structure (and hence function) of macromolecules governed by foundational principles of chemistry and physics?

How are a variety of experimental and computational approaches used to observe and quantitatively measure the structure, dynamics and function of biological macromolecules?

Each question in the framework is associated with a brief overview of the key content features and a series of sample learning objectives. With regard to non-covalent interactions, the key conceptual areas and how they are linked to enzyme structure and function are represented by Figure 3.

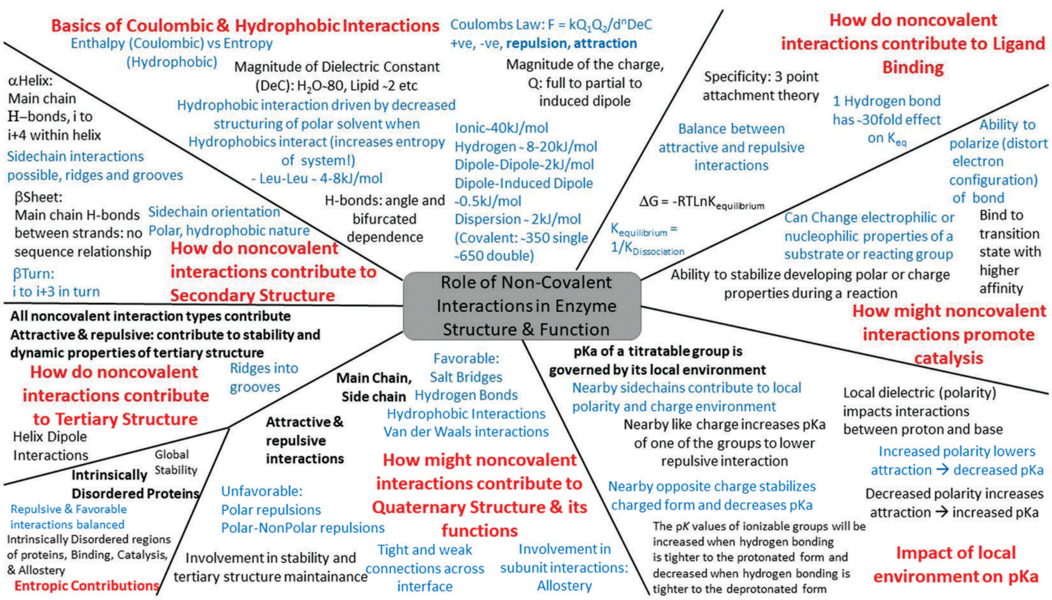

Figure 3. Concept (mind) map of key features of non-covalent interactions and the roles they play in protein structure and function.

This information builds from simple concepts of chemistry and physics and clearly identifies the roles that both attractive and repulsive non-covalent interactions play in enzyme structure function relationships. Interestingly, very few biochemistry textbooks or pedagogical publications (*13*) acknowledge the pivotal role that repulsive non-covalent interactions play in structure function relationships leading to both student and faculty misconceptions about non-covalent interactions.

One of the hardest parts about teaching, whether it is concepts or content or skills is setting the level of expectations of the students clearly. For example, a suitable learning goal for the material represented above could be: "Understand the various roles that non-covalent interactions may play in the structure and function of an enzyme." If this is accompanied by a clear rubric that is given to the students and used in grading any related assignments, it has been shown that student outcomes improve (*14*). A rubric that has been developed by a group of faculty from different institutions tha are part of the Malate Dehydrogenase CUREs community (*15*) is shown in Table 4.

Table 4. Learning Objectives and Assessment Rubric for the *Learning Goal:* "Understand the Various Roles that Non-Covalent Interactions May Play in the Structure and Function of an Enzyme."

Learning Objective	*Category*	*Criteria*
Compare and contrast the physical basis for Coulombic interactions and Hydrophobic interactions		
	Excellent	Coulombic interactions: charge - charge interactions, Coulomb's law, attractive, repulsive, depend upon magnitude of charge, full, partial charges, depends upon surrounding dielectric, distance. Hydrogen bonds may be bifurcated, depend on angle, distance, polarity of partners, strong hydrogen bonds may have some covalent character. Hydrophobic interactions- only favorable, need polar solvent, depend upon entropy of the system, solvent cages around individual hydrophobes decrease entropy, hydrophobic interactions minimize entropy loss. Repulsion effect of polar-nonpolar interactions.
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
Briefly outline the types of non covalent interactions you would expect to stabilize secondary structure in a protein		
	Excellent	Hydrogen bonds- in helix between C=O and N-H in i to i+4 relationship- in beta sheets: between strands, C=O to N-H May get charge or hydrophobic stabilization between side chains in helices (helix wheel, ridges and grooves) but not necessary for formation.
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
Briefly outline the types of non covalent interactions you would expect to be involved in maintaining a functional tertiary structure in a protein. How does this change in intrinsically disordered regions of proteins?		

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Table 4. (Continued). Learning Objectives and Assessment Rubric for the *Learning Goal:* "Understand the Various Roles that Non-Covalent Interactions May Play in the Structure and Function of an Enzyme."

Learning Objective	*Category*	*Criteria*
	Excellent	Hydrophobic core (solvent exclusion), hydrogen bonds and charge -charge interactions, van der Waals interactions. Attractive and repulsive: importance of dynamic structure, intrinsically disordered regions/proteins. For folded proteins attractive > repulsive, but not by much . Usually greater in extremophile proteins. In intrinsically disordered proteins or regions repulsive forces> attractive forces.
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
Proteins may have quaternary structure. What types of non-covalent interactions might you expect to see across subunit interfaces? What functions might these interactions play?		
	Excellent	Wide variety of attractive and repulsive interactions- Coulombic, Hydrophobic, van der Waals: govern stability of interface: attractive > repulsive: Functions: govern symmetry, homo and hetero-oligomers, Allosteric regulation, Protein-Protein Interactions
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
What types of non covalent interactions would you anticipate are involved in substrate binding to an enzyme?- compare the relative strengths of the interactions you suggest		
	Excellent	Van der Waals (steric) – size, Charge-Charge attractions (full and partial), Hydrophobic. Full charges > partial charges and hydrogen bonds- affected by polarity of local environment. Important for specificity as well as affinity- 3 point

Table 4. (Continued). Learning Objectives and Assessment Rubric for the *Learning Goal:* "Understand the Various Roles that Non-Covalent Interactions May Play in the Structure and Function of an Enzyme."

Learning Objective	*Category*	*Criteria*
		attachment theory, etc. Any given ligand may have repulsive as well as attractive interactions.
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
How might non-covalent interactions in a protein-substrate complex promote catalysis		
	Excellent	Catalysis promoted by orientation (correct orientation increases number of productive collisions) and by strain of bonds involved in reaction. Strain may be physical or electronic (strained bonds more reactive-higher energy, less stable, better nucleophile, electrophile. Non-covalent interactions involved with stabilization of the transition state and or destabilization of the ground state.
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent
	Unacceptable	Minimal or no aspects of answer
What types of mutations at nearby residues would you predict alter the pKa of a protonatable group on a protein?		
	Excellent	Ones that change the local environment of the protonatable group: mutations that lower polarity promote protonation, raising the pKa, mutations that increase polarity have opposite effect. Mutations that remove or create formal like charge impact pKa to favor the lower energy (more stable) state: e.g. two adjacent carboxyl groups- one will be protonated, one unprotonated
	Good	Misses 1-2 points of excellent
	Acceptable	Misses 3-4 points of excellent

Table 4. (Continued). Learning Objectives and Assessment Rubric for the *Learning Goal:* "Understand the Various Roles that Non-Covalent Interactions May Play in the Structure and Function of an Enzyme."

Learning Objective	*Category*	*Criteria*
	Unacceptable	Minimal or no aspects of answer

Table 5. Concepts, Content and Skills Associated with Pre-Med Education

Area	*Concepts*	*Content*	*Skills*
Foundational	underlie biological complexity, genetic diversity, interactions of systems within the body, human development, and influence of the environment.	the ability to synthesize information and collaborate across disciplines.	grounding in scientific principles and knowledge
Medicine Related	application of scientific knowledge and scientific reasoning based on evidence. The ability to evaluate competing claims in the medical literature and by those in medical industries. Effective practice of medicine recognizes that the biology of individual patients is complex and variable and is influenced by genetic, social, and environmental factors.	Read the medical and scientific literature of one's discipline, but to examine it critically to achieve lifelong learning. These activities require knowledge and skills in critical analysis, statistical inference, and experimental design. Application of scientific knowledge in medicine requires attention both to the patient as an individual and in a social context.	understanding how current medical knowledge is scientifically justified, and how that knowledge evolves. Curiosity, skepticism, objectivity, and the use of scientific reasoning are fundamental to the practice of medicine. Medical professionals should demonstrate strong ethical principles and be able to recognize and manage potential conflicts of interest. Decision making in medical practice involves uncertainties and risks.

The Impact of "Pre-Med" Education: A Focus on Transferable Skills

As the Vision and Change final report was released, a joint AAMC-HHMI committee released a report "Scientific Foundations for Future Physicians (*16*)," whose main conclusions are summarized in Tables 5 and 6, based upon "Overarching Principles."

While the AAMC-HHMI report is relevant to both undergraduate and medical school education, and can be summarized in the phrase "Context, Collaboration and Communication," many of the skills and conceptual areas (though not in the same level of coverage) overlap those that form the centerpiece of undergraduate education in the molecular life sciences (*17*). The recommendations of the AAMC-HHMI report are also reflected in recent changes in the MCAT exam. Although a Biochemistry and Molecular Biology major is a popular "pre-med" major, the major is designed to serve a wide variety of career goals and prepares students for many different career paths including graduate school in many of the life sciences, other professional schools such as dental or veterinary medicine, or careers in science writing or patent law, as well as direct access to jobs in biotechnology, all of which benefit from the conceptual understanding, content and skills associated with a biochemistry and molecular biology major. Since many pre-med students are not biochemistry and molecular biology majors, a significant question that needs to be addressed is whether a "majors" course in Biochemistry is suitable for these pre-med students. Many Biochemistry and Molecular Biology programs cover the central core of biochemistry in a two or more semester sequence with significant biology and chemistry pre-requisites, however pre-med students from other majors often have not taken these pre-requisites. It would appear that, in those cases, a separate, one semester, "survey" course that includes essential concepts from pre-requisites a biochemistry major would have taken, could be taught for such students. Such a course could also serve as a service course for other science majors, including chemistry majors, who might not have taken the biology pre-requisites a biochemistry major has taken. Such a survey course should be program dependent as the biochemical conceptual understanding and content and skills would need to be paired with the program specific essential concepts from "allied fields" that non-majors may be lacking. An alternative approach would be to communicate transparently to the non-major the concepts, content and skills of the field and how a single semester of a biochemistry series will cover a fraction of these areas. For instance, the first course of the biochemistry series may discuss macromolecular structure, kinetics, and glucose metabolism so that a non-major requiring cell signaling knowledge could compliment the biochemistry experience with another course. Both approaches, depending on resources and student populations served, could be a starting point for addressing biochemistry and molecular biology curricula for majors and non-majors. Meaningful conversations about curricular content should take place between all involved departments and programs to best serve the wide population of students needing to take a biochemistry course.

What Is Modern Biochemistry and Molecular Biology?

Finding a definition of Biochemistry and Molecular Biology in either professional society (ACS and ASBMB) is elusive and perhaps this is as it should be. The closest ASBMB comes to a definition is "*Biochemistry and Molecular Biology are distinguished by their focus on information flow, structure, function and mechanism within overarching biological contexts*" at the start of their discussion of curriculum (*18*). Which can be compared with the ACS statement (*19*) "Members of the Division of Biological Chemistry use the principles of chemistry to assist in the development of a deeper understanding of biological processes." Some have used the term Molecular Life Sciences (*2*, *20*). For example, ASBMB runs a very successful biennial conference entitled "Transforming

Undergraduate Education in the Molecular Life Sciences." Perhaps a suitable definition might be "biochemistry and molecular biology contribute to understanding the processes of living systems at the molecular level," which would bring in the multidisciplinary perspectives particularly of physics and mathematics/computational science to those of biology and chemistry. Such a definition would be consistent with both Vision and Change and recent discussions at both ACS and ASBMB about quantitative aspects of the science. Such a definition would certainly be consistent with recent publishing trends in journals invoking biochemistry and molecular biology with an emphasis on "and" rather than separately defining molecular biology as distinct from biochemistry. This definition would also encompass specialized tracks within a biochemistry and molecular biology degree such as "Chemical Biology", "Biophysical Chemistry" or "Computational Biology/ Biochemistry" or the more traditional Immunology, Microbiology, Cell Biology, Cell Physiology, etc. It would also allow the development of foci on increasingly important topics such as environmental biochemistry, molecular ecology, biotechnology, and molecular neurobiology.

Table 6. Communication Skills Required for the Practice of Medicine

Foundational Skills	• write logically and with clarity and style about important questions across disciplines; • articulate persuasively, both orally and in writing, focused, sophisticated, and credible thesis arguments; • be able to use the methodologies that particular disciplines apply for understanding and communicating results effectively; • approach evidence with probity and intellectual independence; and • use source material appropriately with scrupulous and rigorous attribution.
Medicine Related Skills	Scientific matters can and should be communicated clearly to patients and the public, taking into account the level of scientific literacy of these audiences and understanding the intellectual and emotional responses to medical diagnoses and therapies. For example, physicians should be able to explain to patients: • the complexity and variability of the human body to help them appreciate that there is no single approach to the prevention, diagnosis, and management of disease; • the influence of genetic, lifestyle, and environmental factors in health and disease, as well as the heritability of genetic factors; • in appropriate terms, the technologies for diagnosis and treatment of disease, their relative risks and benefits, and the advantages and disadvantages of alternative choices; • in appropriate terms, the rationale for treatment strategies, including lifestyle changes as well as pharmacological interventions, how the drugs work, their possible interactions with other drugs, their risks and benefits, and alternatives, both pharmacological and nonpharmacological; and • how the brain and other organ systems interact to mediate behavior throughout the lifespan in health and in disease.

Current Curricula Recommendations

In the belief that all professional chemists need to know some biochemistry, the ACS guidelines require that approved programs offer and certified majors graduate with the equivalent of three semester hours of biochemistry (Table 7). Molecular aspects of biological structures, equilibria, energetics, and reactions should be covered in the required biochemistry experience for chemistry majors. Sufficient introduction should be presented so that students can obtain the flavor of modern biochemistry and an appreciation of the important applications in biotechnology.

Table 7. Content Areas Recommended by ACS

	Chemistry Oriented	*Biology Oriented*
Biological Structures and Interactions	Fundamental building blocks (amino acids, carbohydrates, lipids , nucleotides, and prosthetic groups. Supramolecular Architecture	Biopolymers (nucleic acids, peptides/proteins, glycoproteins, and polysaccharides) Membranes
Biological Reactions	Kinetics and mechanisms of biological catalysis; Organic and inorganic cofactors	Biosynthetic pathways and strategies/metabolic engineering; Metabolic cycles, their regulation, and metabolomics
Biological Equilibria and Thermodynamics	Acid-base equilibria; Thermodynamics of binding and recognition; Oxidation and reduction processes	Electron transport and bioenergetics; Protein conformation/allostery, folding, oligomerization, and intrinsically disordered proteins (IDPs)
Practical Topics	error and statistical analysis of experimental data, spectroscopic methods; kinetics, chromatographic separations, electrophoretic techniques, protein purification	molecular biology techniques (including PCR), bioinformatics and –omics, molecular modeling, protein engineering, and isolation and identification of macromolecules and metabolites

Notable in its lists are the absence of Evolution and Homeostasis, two unifying pillars of the Vision and Change Initiative and current ASBMB Curricular recommendations.

While the American Chemical Society does not "offer" a degree in Biochemistry and Molecular Biology, or Biochemistry, or Biological Chemistry, its general degree requirements are more course oriented with regard to content rather than concept oriented, although all of the topics in Table 6 appear in some manner in the ASBMB Biochemistry and Molecular Biology Learning Framework. With regard to skills, ACS lists: 1) Problem Solving skills, 2) Chemical Literature and Information Management Skills, 3) Laboratory Safety Skills, 4) Communication Skills, 5) Team Skills, and 6) Ethics. Although the ASBMB "skills" are laid out with more detail, the only significant difference between the two professional societies is in the context of teamwork and collaboration. Both highlight the need to be a team player (valued greatly by industry), but ASBMB specifically recognizes collaboration which has become a central feature in much modern research and is distinct from teamwork.

The American Society for Biochemistry and Molecular Biology Curricula recommendations remain largely based upon the 2004 curriculum recommendations that first introduced a focus of concepts and skills rather than recommended or required courses, refined by the Vision and Change recommendations to incorporate overarching emphasis on evolution and homeostasis throughout the curriculum, as reflected in Figure 2. The Society approved the"Biochemistry and Molecular Biology Learning Framework" which is published on both the Society web page and Course Source (*14*, *15*).

Accreditation and Student Certification

The American Society for Biochemistry and Molecular Biology initiated a national accreditation (*18*, *21*) for programs offering either a B.S. or a B.A. degree in biochemistry and molecular biology (or closely related majors) with two main goals, 1) to indicate that the program offered a curriculum and used pedagogical approaches consistent with the expectations of ASBMB, and 2) to encourage the use of evidence-based high impact teaching practices. Furthermore, to mark achievement by individual students in such programs they developed an independently scored exam aligned with the vision of biochemistry and molecular biology described earlier (Figure 2) that could be used to assess student performance. Students, based upon their performance in the exam, have their degree certified by ASBMB. Students with exceptional performance on the exam are recognized by ASBMB as having graduated with distinction.

The Certification Exam is based primarily on a free response format with minimal or no multiple-choice questions and is designed to be taken in a one hour period. The exam emphaseizes overarching concepts and critical thinking skills, and students are expected to demonstrate the ability to synthesize information into coherent responses, not simply retrieve facts. The exam has twelve to fourteen questions drawn from the four core concept areas illustrated in Figure 2 focusing on evaluation of concepts and competencies outlined in the ASBMB learning goals and objectives.

Results from an independent, nationally-recognized exam not only assist faculty and programs in meeting the demands from accrediting bodies and university administrators for evidence-based assessment, but also provides formative assessment data on areas of curricula strengths or weaknesses.

The use of an independently graded exam covering foundational concepts and skills by the American Society for Biochemistry and Molecular Biology to certify individual student degrees is distinct from the American Chemical Society approach of "certifying" student bachelor's degrees solely on the basis of having been conferred by an ACS approved department.

The Central Role That Undergraduate Research Plays in Undergraduate Education in the Molecular Life Sciences

The Vision and Change Report emphasized the need to incorporate undergraduate research into the curriculum of life science majors. Research experiences have major effects on persistence in science (*22–28*) and positive outcomes in conceptual understanding and skills development, essential for effective workforce development (*29–35*). The Council on Undergraduate Research (CUR) defines undergraduate research as inquiry or investigation conducted by undergraduates that makes original intellectual or creative contributions to the discipline (*36*), and can often be provided by Course Based Undergraduate Research Experiences (*37*). Such work is a high impact practice providing robust service learning for students, increases retention, and enhances student learning though mentorship by faculty. Furthermore, it develops a deeper critical thinking ability, as well as intellectual independence. Realization that authentic research was important for student development was evident in the Boyer Report (*3*), where smaller schools that provide research mentoring disproportionately produce more graduate school students than research intensive institutions.

The central role that undergraduate research plays in the education of students in the molecular life sciences is accepted and well documented. Both the American Chemical Society and the American Society for Biochemistry and Molecular Biology encourage the incorporation of undergraduate research in the curriculum. The format that undergraduate research experiences take varies significantly depending upon the nature of the institution. In institutions with large numbers of students in the major, providing research experiences for all students presents problems. Flexibility in the ways that research experience is gained is essential. This experience might be obtained by mentored research in the research lab. Alternatively, it could be via a summer research experience or through course-based undergraduate research. Course-based undergraduate research experiences (CUREs), as will be discussed in a separate chapter in this volume, provides a cost-effective way of engaging all students in research activities. The benefits of undergraduate research have been extensively studied and documented, and as discussed earlier undergraduate research is regarded as a high impact teaching practice (*38*). To inclusively provide a research experience to students, faculty and institutions will need to take advantage of all models of undergraduate research to more widely deliver this high impact experience to all students.

Research experiences should engage the student in all aspects of research. The work of Dolan and others have established criteria that are the hallmarks of research (*39–42*). These include, as illustrated in Figure 4, student generated hypotheses and original research that provides new knowledge.

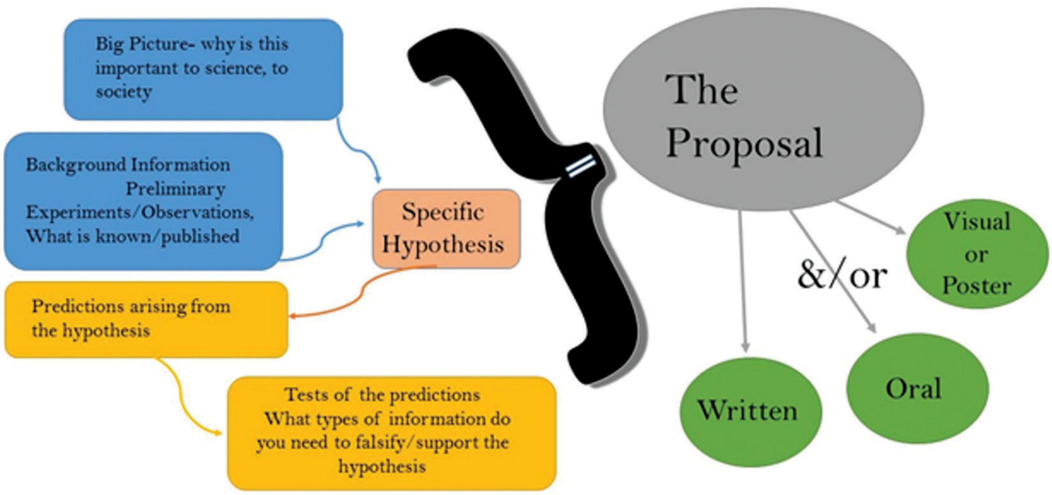

Figure 4. Essential elements in a student generated research hypothesis and proposal.

This requires a number of abilities including access to prior knowledge and the ability to assess the validity of information. Participation in authentic research activities also provides students with the opportunity to present their work in a variety of formats, using a variety of communication skills. Undergraduate research should include opportunities to write formal research proposals, and, of course, final reports that may be in the format of contributions to the scientific literature.

As with the earlier example of no- covalent interactions, providing students with a detailed rubric, Table 8 (developed by the Malate Dehydrogenase CUREs Community (*15*)), lets students know the level of expectation and detail that they should achieve.

Table 8. Learning Objectives and Assessment Rubric for *Learning Goal:* Create/Develop and Present a Testable and Falsifiable Hypothesis and Appropriate Experiments to Interrogate the Hypothesis

Learning Objective	*Category*	*Criteria*
Describe how the proposed work fits into the field/fills a gap in knowledge		
	Excellent	Relationship of big picture of project to the field clearly indicated and explained
	Good	Relationship of big picture of project to the field indicated but explanation unclear
	Acceptable	Relationship of big picture of project to the field clearly mentioned but not explained
	Unacceptable	Relationship of big picture of project to the field not addressed
Clearly states their Hypothesis and the requisite background information that lead to the hypothesis		
	Excellent	Hypothesis or goal clearly stated. Gives appropriate background justification for hypothesis
	Good	Hypothesis or goal clearly stated but lacking justification
	Acceptable	Hypothesis or goal is not clearly stated. Cited studies cited may or may not support hypothesis or goal as written.
	Unacceptable	Hypothesis or goals lacking
Clearly indicates the testable and falsifiable predictions the hypothesis makes		
	Excellent	Clearly states and justifies testable and falsifiable predictions and relates to hypothesis. Indicates controls
	Good	Limited predictions and justifications, some indication of controls
	Acceptable	Limited predictions, no justification or controls indicated.
	Unacceptable	Predictions lacking
Briefly outlines the types of experiments and data that will be used to interrogate the hypothesis		

Table 8. (Continued). Learning Objectives and Assessment Rubric for *Learning Goal:* Create/Develop and Present a Testable and Falsifiable Hypothesis and Appropriate Experiments to Interrogate the Hypothesis

Learning Objective	*Category*	*Criteria*
	Excellent	Summary of experiments is consistent with testing hypothesis or reaching goal. Types of data that will support or falsify hypothesis indicated
	Good	Outlines experiments but not how the data will contribute to the interrogation of the hypothesis
	Acceptable	Gives detail but some proposed studies are not consistent with hypothesis or goal.
	Unacceptable	Minimal attention to how experimental data will be obtained or used to interrogate the hypothesis
As appropriate cites necessary references		
	Excellent	References added appropriately
	Good	References placed in text but some references missing.
	Acceptable	Significant omission of references.
	Unacceptable	R writteneferences lacking.
General flow/organization		
	Excellent	Logical flow from global to particular study point of view. Engaging writing style. Clearly connects ideas. Good use of graphics
	Good	Solid order and structure. Inviting writing style. Effectively moves the reader through the text. Graphics present but not well explained
	Acceptable	Organization is functional; some order lacks logical pattern and structure. Minimal use of graphics
	Unacceptable	Lacks cohesive structure, difficult to follow.
Grammar/spelling/general attention to detail		
	Excellent	No spelling or grammatical errors; includes all required sections; clearly written in language for reader familiar with biochemistry; well organized and legible
	Good	Minor spelling or grammatical errors; includes all required sections.

Bussey et al.; Biochemistry Education: From Theory to Practice
ACS Symposium Series; American Chemical Society: Washington, DC, 2019.

Table 8. (Continued). Learning Objectives and Assessment Rubric for *Learning Goal:* Create/Develop and Present a Testable and Falsifiable Hypothesis and Appropriate Experiments to Interrogate the Hypothesis

Learning Objective	*Category*	*Criteria*
	Acceptable	Some spelling and grammatical errors; some sections not complete or less well organized.
	Unacceptable	Significant spelling and grammatical errors; disorganized, difficult to follow.

Bussey et al.; Biochemistry Education: From Theory to Practice
ACS Symposium Series; American Chemical Society: Washington, DC, 2019.

Experiential Learning

A critical role in the education of biochemistry majors is also given to experiential learning. This can take a variety of formats including laboratory courses, service learning, and internships and should include laboratory safety and the recognition of common laboratory hazards and responses to accidents involving hazardous materials. Reiterative discussion of the principles of ethical conduct of research and scholarship, (plagiarism, appropriate citation, qualifications for authorship, appropriate use of images and confidentiality) should be embedded in appropriate classes. In all cases of experiential learning, there should be a common intellectual thread through the activity, where the student has ownership, engages in appropriate science-related activities, and is required to document and communicate that work.

Whether with undergraduate research or experiential learning the activities should constitute a significant component (ASBMB recommends a minimum of 400 contact hours, ACS 400 hours beyond introductory chemistry laboratory) and be distributed throughout the curriculum.

A Student-Centered Curriculum

The Vision and Change report emphasizes the use of evidence-based teaching approaches where studies have shown that the classroom approach actually leads to student gains. Further-more, Vision and Change emphasized the need for an active, student centered classroom. A number of studies over the years have suggested that the traditional lecture approach to teaching is not particularly effective. Despite growing evidence supporting the effectiveness of a wide variety of high impact, student-centered approaches (*43–49*), lectures still dominate the teaching profession. A recent study suggested that 55% of teaching involves traditional lectures with a further 25% involving some sort of lecture format (*50*).

Figure 5 illustrates a variety of student-centered approaches where evidence has shown the approaches to be effective in the classroom. These include Think-Pair-Share activities (*43*), the use of clicker questions (*44*), peer teaching (*45*, *46*), case study use (*47*), and the use of student modeling activities (*48*). A particularly effective approach involves so-called brainstorming, which is sometimes referred to as mind mapping or concept mapping (*49*). Other approaches include reflective writing (*51*), peer review (*52*), collaborative work (*53*), the so-called one minute paper (*54*) (where students write a summary of a brief lecture or create a concept or mind map), portfolios (*55*), service learning (*56*), and learning communities (*57*)). In all cases, these approaches actively involved students or groups of students in developing and reviewing information and concepts. Here we will discuss briefly several of these approaches which we have found to be particularly effective in our biochemistry classes. These are Think-Pair-Share activities, peer teaching, peer-review, and the use of concept or mind maps.

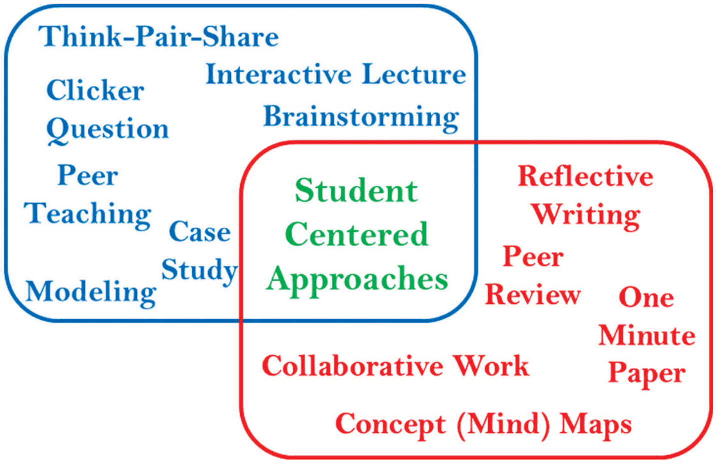

Figure 5. Student centered high impact teaching practices.

Think-Pair-Share

Think-Pair Share activities involved the instructor asking a question and giving the students in the class several minutes to think on their own and make notes about the question. The pair component of the activity involves students forming pairs or small groups and discussing the individual responses to the question. The group then decides on a consensus setoff points for the question. In the share component, a member of the group shares this consensus with the class. The share component often involves the instructor revealing the correct answer.

Peer Teaching

Based on the old Chinese proverb "*Tell me and I'll forget; show me and I may remember; involve me and I'll understand,*" peer teaching is a variant of the SODOTO approach (See One, Do One, Teach One) often used in Medical Schools (*58*) and related to Think-Pair-Share approaches. In peer teaching, a topic, perhaps represented by a paper from the original literature, is used as the basis of the peer teaching activities. The classroom is split into groups and each group assigned a particular aspect of the paper perhaps represented by a figure or table in the paper. The groups are given a period of time to discuss what features of the topic are essential to understand the topic. Each group then designates a "teacher" who will carry that information to the next group and teach the group the agreed-upon topics. This process continues during the class until all groups have discussed each topic. In the process, all students have played the role of both learner and teacher and had to think about how best to present the material. The faculty member listens in on the various discussions throughout the class and adds appropriate information as needed. Usually the class ends with a brief summary of the pertinent information on each topic.

Peer Review

Peer review activities are particularly appropriate for either laboratory classes or classes that involve significant writing components. Students, often as a homework assignment have written a paper on the assigned topic. The papers are collected, anonymized, and given to students to peer review (usually 2-3 per student). The review usually involves a detailed rubric and the reviewing students assign scores based upon the rubric. To be truly effective, the peer-review culminates in class presentations of the strengths and weaknesses of each paper and depending upon the context can involve students ranking the papers based upon the scores they gave using the rubric. The instructor plays the role of agent provocateur, raising appropriate points as needed to direct the class discussion. For each paper reviewed, one student in the class is designated the "recorder" and is tasked with summarizing the points, good and bad, raised during the class discussion of a given paper. This type of peer review approach allows students to see and discuss a wide range of writing styles and actively decide which approaches are the most effective. After the peer review of all the papers, each student is given the blind reviews of their own paper and the recorders summary of the class discussion and has the chance to revise their paper before submission for grading. Such peer review approaches work particularly well with CURE based laboratory classes where students formulated their background information, a hypothesis, and predictions that can be explored experimentally.

Mind Maps

The construction of concept maps or mind maps requires students to be actively involved in creating connections between concepts or topics, and in organizing information in a logical manner. For example, prior to class, students can be assigned reading on the topic, and, at the start of class, are grouped and asked to create a mind map of some aspect of the topic. Each student group then presents their mind map on the assigned topic using, for example, a white board. The groups then rotate through all of the mind maps and are asked to add any comments they think necessary to improve the original mind map. After all of the groups have visited and commented on all of the mind maps, the groups returned to their original mind map and, as appropriate, revise the mind map. At the end of class, all of the mind maps are photographed (students always have their smart phones with them), and the photographs sent to the faculty member who then posts them to a class website. As appropriate, the faculty member also creates and circulates idealized mind maps of each topic presented in the class. For example, Figure 6 is a consensus mind map generated from in-class discussion of the basics of reactions and interactions necessary to understand enzyme function which aligns concepts from chemistry with enzyme function.

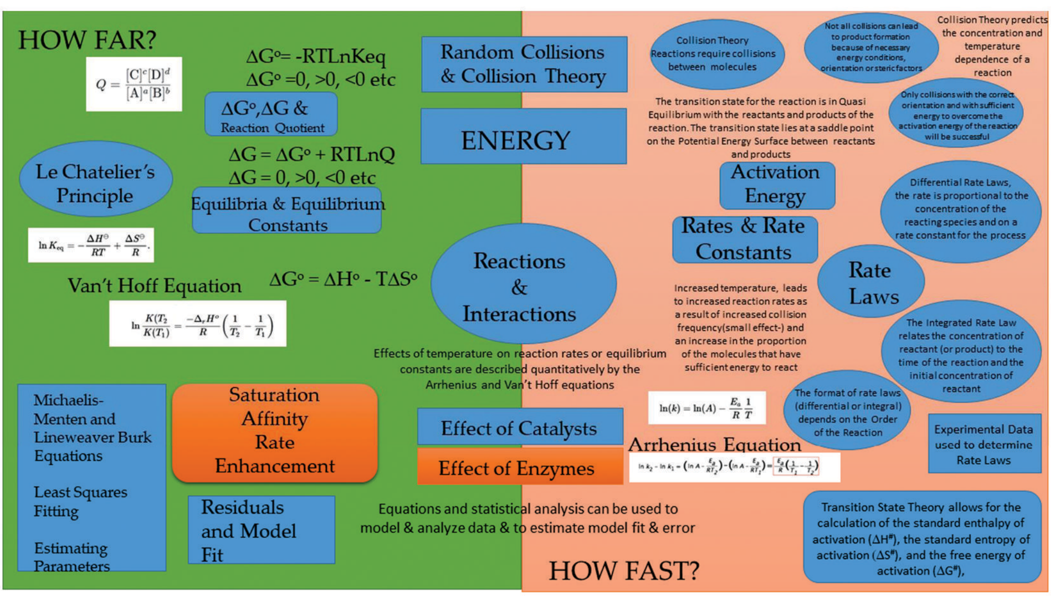

Figure 6. Consensus mind map of central concepts of reactions and interactions generated from class discussion.

Using mind maps in this way effectively combines aspects of peer teaching, Think-Pair-Share activities, and peer review.

The Problem of Large Class Size

Although large class sizes are sometimes used as a justification for keeping to a traditional lecture format, in reality many of the high impact teaching practices suggested in Figure 5 and discussed here are easily incorporated into a large class format, and have been at a number of large institutions. Think-Pair-Share, Clicker Questions, Concept Mapping, Case studies and One Minute Paper ideas all translate essentially seamlessly to a large class format particularly when combined with well thought out rubrics, well trained teaching assistants and recitation or Review sessions. Many large universities (for example, the University of Texas) that routinely face the problem of large class sizes have centers for teaching and learning that prepare faculty and teaching assistants, and publish resources that are freely accessible to all faculty (*59*).

Gateway Concepts

In recent years, there has been significant discussion of "Gateway" concepts (*60–63*) and a number of so-called concept inventories have been developed (*64–69*). Gateway concepts are ideas and theories that are foundational to understanding the biochemistry that is built from them. For example to understand the structure-function relationship of macromolecules students must have a firm grasp of at least 5 gateway concepts of chemistry (see below), and with this foundational knowledge, students should readily be able to evaluate macromolecular structures in terms of through bond and through space interactions. Likewise, understanding enzyme kinetics and regulation builds from foundational chemistry concepts of reactions and interactions.

Some discussion of the core concepts of the "allied" fields that set the stage for biochemistry and molecular biology seems warranted.

The structure (both in terms of through bond connectivity (covalent bonds) and through space interactions (non-covalent interactions, both favorable and repulsive) of a molecule determine its dynamic properties and reactivity (chemical and physical): i.e. its function. Five gateway concepts of bonding and interactions underlay the foundation for understanding macromolecular structure function relationships and the structure, activity and regulation of enzymes. These are: 1) Core Concepts of Covalent Bonds and Polarity, 2) Bond rotations and vibrations , 3) Hydrogen bonds and other non-covalent interactions, 4) The Hydrophobic effect and 5) Dynamic aspects of molecular structure. Likewise, there are a series of gateway concepts for understanding reactions.

Enzymes are biological catalysts that enable cells to control the wide variety of chemical reactions that continuously occur in a cell. Enzymes enable these processes to occur at ambient temperatures, with the requisite specificity, and unlike chemical catalysts, exhibit the phenomenon of saturability. The reactions catalyzed by enzymes often have mechanisms for regulation of the rates of the reactions. While many enzymes are proteins, some RNA molecules also exhibit enzymatic activity and are termed "catalytic RNA." In all cases, the interactions of enzymes with their substrates, products and, if appropriate, regulatory molecules are governed by the same foundational concepts that govern chemical reactions in general. Presented here are 5 "gateway" concepts necessary to understand the action of enzymes from a chemical perspective. 1) Collision theory, 2) Transition state theory, 3) Rate laws, Steady States and Equilibria, 4) The effects of temperature, and 5: Structure and reactivity.

These gateway concepts are expanded in more detail in Appendix 1.

Understanding Student Misconceptions of Gateway Concepts Can Lead to More Effective Instruction

Over the past 15 to 20 years there has been a significant effort on developing so-called concept inventories in biochemistry and molecular biology. Unfortunately, often these do not reflect the underlaying concepts, but are useful tools in developing an understanding of student misconceptions. Significant work on identifying student misconceptions in certain key areas of biochemistry and molecular biology have contributed to improved teaching approaches. To have a maximum effect on student outcomes, it is essential to link foundational or gateway concepts to effective assessment of student outcomes and identification of student misconceptions (Figure 7). This requires identification of the Threshold (Gateway) concepts at the level of introductory classes in Chemistry, Biology, Physics, and Mathematics and how they feed into introductory concepts of biochemistry and molecular biology. The work of Loertscher and Minderhout and colleagues (*60–69*) is an important starting place, but more work, especially in the areas of chemistry and mathematics, is needed. Allied with identification of such gateway concepts is the need for suitable assessment instruments capable of identifying student misconceptions, as discussed by Lewis and coworkers (*66*).

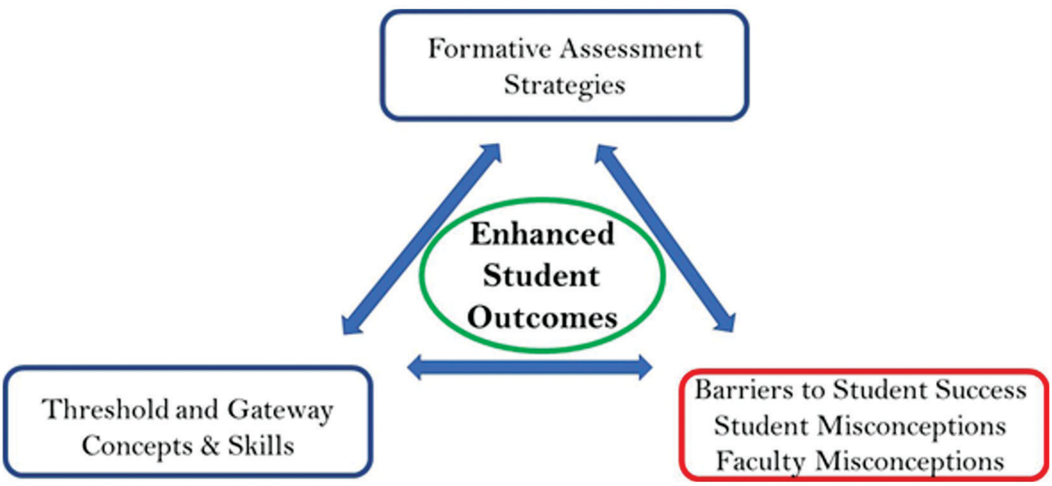

Figure 7. Enhancing student outcomes Through a cycle of formative assessment of foundational concepts and skills.

Finally, as demonstrated by and emphasized in the work of Taylor et al. (*70*), it is necessary to continually reinforce all areas of conceptual, gateway knowledge that has been introduced in prior course work to enhance student retention. This can be in the form of using a "pre-test" at the start of a course based upon pre-course reading and review of "assumed" knowledge, or a brief bootcamp to quickly review such assumed knowledge.

Quantitative Skills in the Curriculum

Figure 8 summarizes the quantitative skills that are essential for biochemistry and molecular biology.

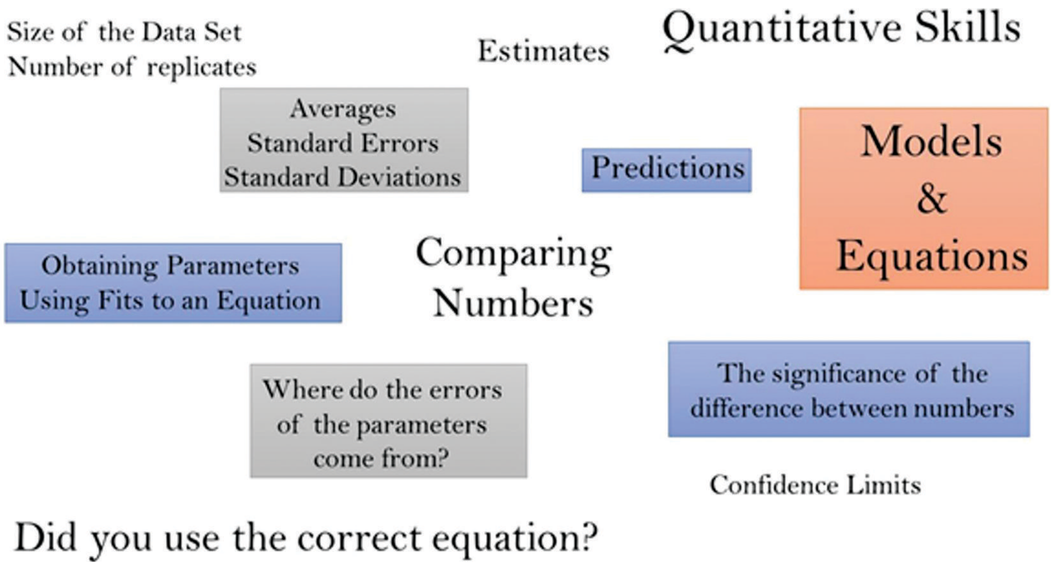

Figure 8. Key elements of quantitative skills for biochemistry and molecular biology.

While a number of articles and reports, including BIO2010 and Vision and Change, have emphasized the need for undergraduate students to be better educated in the area of quantitative mathematical models of biological phenomena to enable them to engage in an era in science increasingly dominated by "Big Data" (the Omics era and topics such as Genomic Enzymology), this is still an area of deficit. Students in the molecular life sciences seem increasingly "equationophobic" and generally have poor quantitative skills and intuition. It seems that, as a community of biochemistry and molecular biology educators, we assume that students are "learning" these quantitative skills elsewhere in the curriculum. We need to do better. The argument seems too often to be that 1) there is too much material (content) to cover, 2) we don't have time to focus on those quantitative, 3) students should have acquired these quantitative skills elsewhere. Many faculty have a "bootcamp" week at the start of a course where they review essential background. Perhaps this idea should be extended to include a "quantitative methods" bootcamp at the start of every course in the molecular life sciences. Quantitative skills can be developed, allowing these skills to be fully integrated across the curriculum. As with foundational concepts, repetition is the key to student comfort, familiarity, and retention of these skills.

Communication: Writing and Presentation Skills

Communication skills are highly valued by almost all employers, irrespective of the field of employment. Developing various forms of communication in the course of a student's education is known as a high impact practice (38). The training of undergraduates in Biochemistry and Molecular Biology offer a wide variety of formats for student engagement in communication, as summarized in Figure 9, and can be incorporated in many ways throughout the undergraduate curriculum.

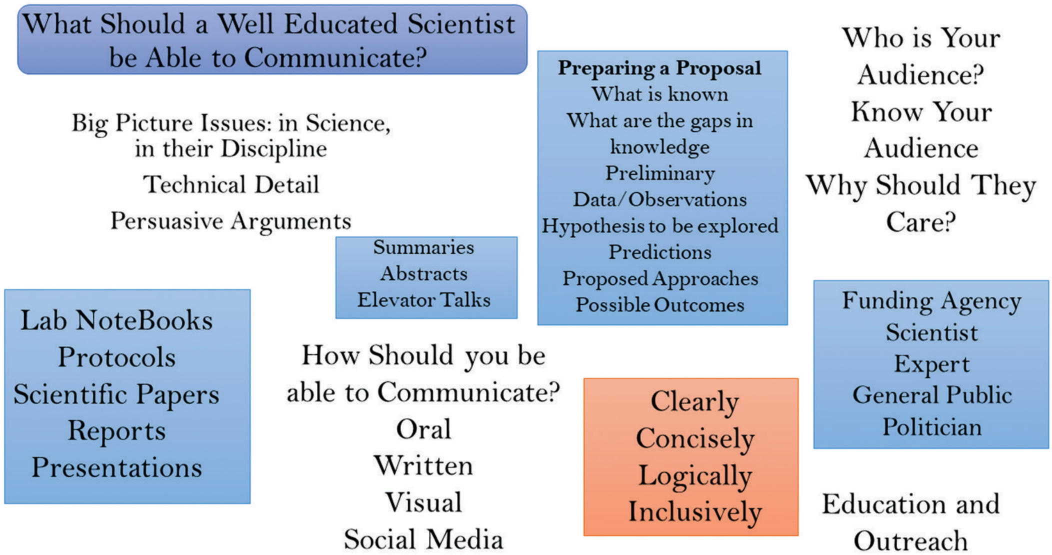

Figure 9. Key elements of communication come in many forms with various audiences.

Whether in written, oral, or visual formats students should be able to communicate to a variety of audiences, and in today's world should also be aware of how to communicate using a variety of social media formats. Developing the attributes of great communicators lays the groundwork for success, not only in the classroom, but also in one's life and career. These attributes can be put into the three components of communication, When, What and How: 1)When: To be an effective communicator, someone must listen and be able to both understand and know when to respond appropriately, they must be able to relate to others and tailor their message to the audience at hand, they must be available and able to lead inclusive discussions and they must be able to ask questions that engage the audience and give some level of ownership to the audience for the answers. 2) What: They must be able to simplify the complex and make the complicated understandable. They must be specific, clear and concise, and on point so that the audience doesn't have the opportunity to be distracted by off message points. And 3) How: They must be confident to earn audience trust and demonstrate their knowledge, and they should be audience appropriate in terms of body language and attire. In terms of the life sciences, the various types of "things" a student should be able to communicate, as well as the different audiences they should be able to communicate with, are summarized in Figure 9. Opportunities for such communication should be threaded throughout the curriculum (*71–74*).

The Central Role That Accessing and Assessing Knowledge Plays in Undergraduate Life Science Education

In addition to conceptual areas of the science and foundational skills, to prepare students for the ever expanding content of life science disciplines, and the challenges of the workplace or graduate school, it is essential that the undergraduate curriculum include both exposure to current issues and advances in the science and arm them with the skills to assess the information that they hear/see/find. As summarized in Figure 10, undergraduates should be aware of and use original peer reviewed literature, they should be able to access and use publicly available data (structural, sequence, and -omics data), and understand the conceptual basis of computational approaches such as quantum mechanics, molecular mechanics, and molecular dynamics. There are many ways that these aspects can be incorporated into the curriculum including regular outside speaker seminar series, student/faculty journal clubs, and seminar courses that involve a series of "current topics."

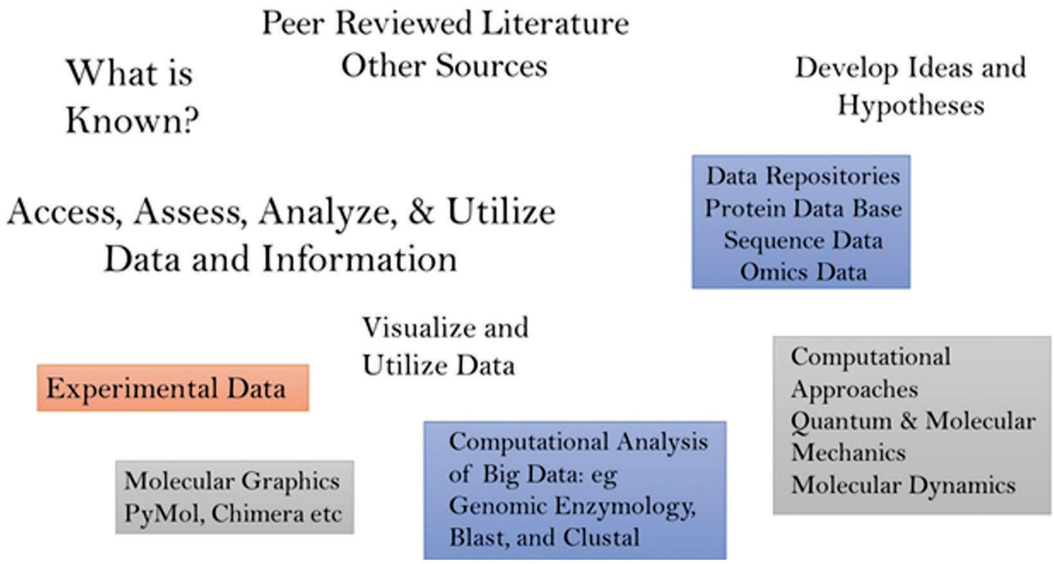

Figure 10. Students must access, assess, analyze and utilize data and information from many sources in biochemistry and molecular biology.

The Important Role of Capstone Courses and Experiences

Many of the pedagogical approaches discussed here are often incorporated into a capstone course or experience. Capstone courses play a significant role in helping students not only hone essential skills, but also integrate material from other courses. Capstone courses are often writing intensive courses which also augments communication skills (*75–77*).

Content versus Concept Revisited

With a focus on conceptual knowledge rather than extensive content, a question arises as to whether there are certain areas of biochemistry and molecular biology that must be included as content areas in the curriculum. It can be argued that if student understanding of the concepts can be assessed, detailed knowledge of specific content areas should not be required, although detailed knowledge of instructor chosen areas leads to deeper student understanding. For example, if the concepts required for an effective signaling pathway are understood and can be recognized by a student, is it necessary that any given signaling pathway be covered? If the ways that an enzyme can enhance the rate of a reaction and be regulated is understood at a conceptual, mechanistic, quantitative way, does it matter whether the enzyme is Phosphofructokinase or Aspartate Transcarbamoylase? Exceptions, because of their universality, might be how ATP is synthesized, and how DNA is replicated, transcribed and translated. If metabolism is understood at a big picture level in terms of the needs of an organism and how homeostasis is maintained at a conceptual level, do we need students to demonstrate detailed understanding and knowledge of specific pathways rather than illustrate their conceptual understanding with specific knowledge?

It also raises the issue of how to best assess student understanding. Traditionally, exams have been based largely on content, rather than conceptual knowledge. The changed focus to concepts suggests that we need to rethink how we measure student outcomes. It also suggests that we rethink the way we assign grades in courses. In many courses, the large majority of the grade is based on periodic exams. Depending on the frequency of such exams this simply encourages student memorization of content. The American Society for Biochemistry and Molecular Biology is attempting to change this paradigm with its national accreditation exam which focuses on the conceptual areas of the learning framework approved by the society. Although this is a national exam not intended for incorporation into a course, nor designed to contribute to a student's grade, it is groundbreaking with its focus on conceptual areas. As faculty we need to think about how to use such an approach as a component of our grading of students. As part of the move towards concepts and skills, it is important that we appropriately reward students for demonstrating their understanding and abilities. This suggests that the overall grade in a course should be based on a wide variety of assessments, not just on content-based exams. While there will always be a place for the traditional exam in most courses, this is not always the best way to assess student understanding of concepts or reveal misconceptions. Written exams are also not ideal for assessing many required skills and, depending upon the learning goals and objectives of a course, a variety of assessment tools should be used to assign grades. Consider the principles of backward design where one starts with what you want the students to be able to do, then determine the best way to assess whether the student can in fact do it, and finally establish the preferred way of "teaching" the student (*78*). This suggests that the best way to assign grades should mimic the ways that give evidence of student success at mastering the learning objectives or goals of the course. Even with traditional exams, the focus on conceptual knowledge and understanding should be reflected in the style and wording of the questions used. Too often, exams focus on lower level Bloom's taxonomy types of questions, focusing on memorization, rather than conceptual questions which require higher level Bloom's taxonomy responses and involve applying, analyzing, evaluating and creating conceptual understanding. Such questions usually provide information to the student rather than requiring memorization of content, and ask the student to apply conceptual understanding. As part of any discussion on "grading," the role of rubrics for assignments cannot be overemphasized. Students should be provided with clear expectations. Well-constructed rubrics for graded assignments let a student know what is expected of them. (*14*). The skills, conceptual understanding, and content areas we want our students to get from our classes and curriculum should be demonstrated and modeled in our classes and laboratories. While on the topic of exams, it is important to point out that educational research (*79*) has shown that spacing and repetition of delivery of material and assessment of student understanding can play an important role in long term student understanding rather than short term memorization. If we want students to understand and utilize foundational concepts, these concepts should be re-emphasized, with students applying the concepts in a variety of settings, and their understanding of them assessed, throughout the curriculum. Teaching concept or content one week and assessing it the next and moving on to the next topic does not lead to long term understanding and ability to apply the concept to new situations.

Biochemistry and molecular biology degree programs usually build from a base of introductory courses from other departments such as chemistry biology physics and mathematics. This is unfortunate, since the foundational concepts that biochemistry and molecular biology build from are usually introduced in courses that have no intentional biochemistry and molecular biology content or focus. As a result, students effectively silo introductory concepts from the "allied field" disciplines away from biochemistry and molecular biology, which they often first see only as juniors. To fully realize a biochemistry and molecular biology degree, it is essential that these introductory and gateway concepts to molecular understanding are taught in the context of biochemistry and molecular biology, the molecular life sciences.

The truly interdisciplinary nature of biochemistry and molecular biology, emphasized in both the Vision and Change report, and by the American Society for Biochemistry and Molecular Biology, has led in some institutions to the creation of introductory interdisciplinary courses. Such courses have the capability of illustrating to the students the interdisciplinary basis that underlies the molecular life sciences. At one extreme, courses have been created where for example 5 faculty, representing biology chemistry, mathematics, computer science, and physics, coteach an introductory course that not only lays the groundwork for further coursework in each of the disciplines, but addresses topics in the molecular life sciences in a cohesive interdisciplinary manner (*80–82*). Such courses lead not only to students that appreciate the interdisciplinary nature of most of the sciences, but also students able to readily cross the boundaries between the disciplines in their own studies and research. Other courses have been developed that link two disciplines to the benefit of both (*80–82*). For example, a faculty member teaching an introductory chemistry course might team up with a faculty member teaching an introductory biology course, and both courses emphasize the cross disciplinary connections. Although such approaches are clearly beneficial to the students, it is often difficult to create such courses because of the siloed nature of departments, teaching loads and financial constraints.

Finally, whether we discuss biochemistry and molecular biology in terms of concepts or content, the question we really must answer given the realities of today's universities and colleges, is what courses do we put in the curriculum. In terms of biochemistry and molecular biology, one can argue that overall there are three types of courses that we must teach. 1) There are courses that are required for the major, 2) there are courses that are in effect service courses for other majors, and 3) there are courses that will fulfill the science requirement for non-science majors. With regard to courses for biochemistry and molecular biology majors, as a result of the discussions associated with Vision and Change and endorsed by both the American Chemical Society and the American Society for Biochemistry and Molecular Biology, there is general agreement as to the conceptual areas that should be covered. How courses are structured to cover both the conceptual areas and skill areas necessary for today's students is, and should remain, logically a departmental or programmatic decision. While biochemistry and molecular biology degrees offered by either chemistry or biology departments often have a more chemical or biological focus, the discipline is best served by cooperation and collaboration between the departments. When the degree is offered by a standalone biochemistry and molecular biology department, there is still a need for discussion and collaboration at the level of the introductory courses.

To cover the requisite concepts skills and appropriate content in the major clearly requires more than a single semester course. When considering how a program fulfills its service teaching requirements to other departments or programs, it becomes a question as to whether, for example, students taking a biochemistry class as a non-major should take the same class that a biochemistry and molecular biology major would take. Practically speaking, the biochemistry and molecular biology major is best served by a sequence of courses with the requisite labs, as appropriate, that cover the topics identified by the major professional societies. So, the question becomes should a non-biochemistry and molecular biology major simply take one of this sequence of courses and expect to be well served for their own particular major. The answer would seem obvious - no..

What becomes of courses designed for non-science majors. Virtually every science department teaches one or more courses that are designed for non-science majors. The question that all science departments, colleges, and universities should ask is. "What do we want the average citizen to understand about science?" It should not be some physics, or any other specific science, but an understanding of what science is, and what science is based upon. Just as most science is becoming more interdisciplinary a strong argument can be made that the average non-science student should have knowledge not only of how science is structured and how science is conducted, but also the big ideas and issues facing each of the disciplines. Conceptually this suggests that science requirements for all non-science majors should not only promote understanding of the scientific approach, but also present these big ideas and issues at a conceptual and understandable level for all students. Biochemistry, as an inherently interdisciplinary science might be particularly suitable for a non-science majors course and often forms the core of laboratory based non science majors courses that introduce students to the approaches and practices of science in general. Furthermore, such courses do not need to develop the student skills appropriate to all majors since those skills should be developed in the context of the students major, that is, in courses specific to a particular major, offered by the home department.

Foundational Concepts of Interdisciplinary Science for the Molecular Life Sciences

To be truly effective, the interdisciplinary aspects of science need to focus on overarching interdisciplinary concepts rather than simply take disciplinary terms and discuss them from multiple perspectives. In the Biochemistry and Molecular Biology learning framework, interrelated interdisciplinary concepts are introduced as outlined in Figure 11 Each of the conceptual areas (Figures 1 and 2) that make up Vision and Change or biochemistry and molecular biology benefit by inclusion of these interdisciplinary concepts, which focus students on broader conceptual understanding and principles of design and function of living systems.

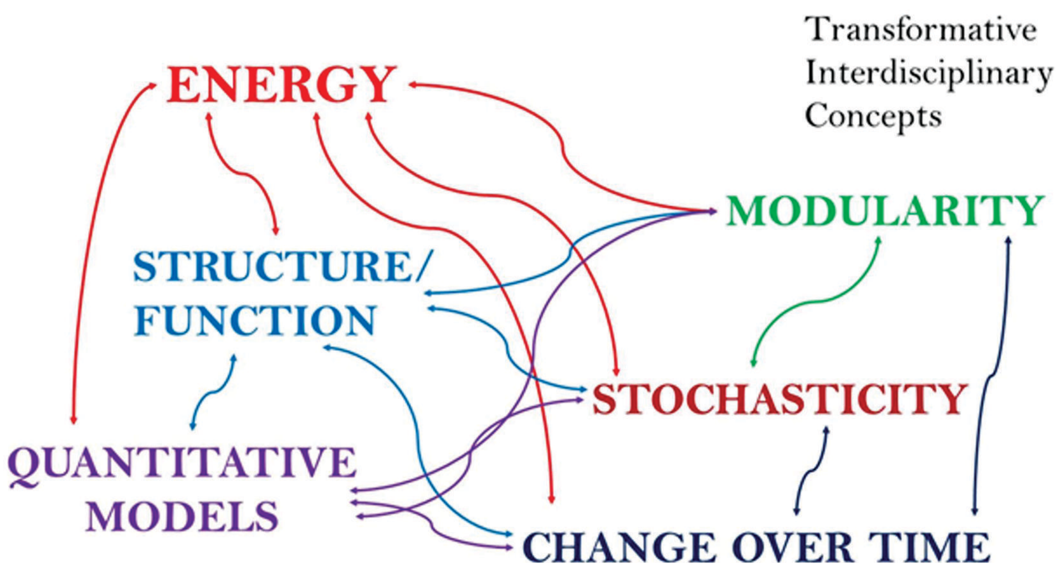

Figure 11. Overarching interdisciplinary concepts can provide a lens to examine all aspects of biochemistry and molecular biology.

How Could the Ideal Curriculum be Structured?

As discussed throughout this chapter, there is much common ground between the two major professional societies dealing with undergraduate biochemistry and molecular biology education. While these areas of agreement focus on concept/content areas and skills, it is worthwhile to think about how in an ideal situation a curriculum could be structured.

Recognizing that first year introductory courses must set the concept/content stage for multiple majors (Chemistry, Biology, Biochemistry and Molecular Majors, Other Life Science Majors) as well as excite students about science and introduce the requisite skills to allow students to successfully start undergraduate research, we would suggest that the first year curriculum contain at least one course that focuses on big picture issues that face the life sciences, and one course that emphasizes the scientific process and skills necessary for students to start research. Finally, as either a stand-alone course, or as a significant component of another required laboratory course, students should be engaged in CURE activities where they engage in hypothesis development and other research-oriented skills. Other courses in the first year should emphasize the interdisciplinary and conceptual areas that underlay what are often referred to as the "allied fields" of chemistry and biology, with a strong focus on quantitative and mathematical skills.

The second year should build upon these foundations and contain a "Gateway" course that sets the stage for Junior level courses in biochemistry and molecular biology. This gateway course could be paired with a laboratory sequence that introduces students to common techniques as well as bioinformatics and computational approaches that increasingly play important roles in the molecular life sciences. Integrated into such a gateway course should be outside speaker seminars highlighting a variety of career options, and discussion of research activities within the department/program, etc.

During the junior year, students should be completing all of the required concept/content area courses that form the core of the major and continuing research activities (either as a CURE or as mentored research) or participating in appropriate experiential learning activities. Regular research seminars and further career orientation activities should be integrated into a required course to ensure that all students participate in these critical activities.

Senior year should be devoted to electives within the major, and/or a capstone course and continuation of research activities or experiential learning activities, which should culminate in a presentation as part of a required "senior seminar".

To be successful and to allow students to benefit to the fullest extent, the curriculum for the major, or the overall curriculum for the students should not be so crowded that students cannot participate in research or experiential learning in a meaningful way, and do not have the time for reflection necessary for them to take charge of their own education and prepare for lifelong learning beyond their bachelor's degree. Courses and degrees in the molecular life sciences should be designed to encourage/allow/prepare students to think and act like scientists and open doors to careers where students can utilize their passion for science in the ways that they choose to do so.

The Critical Role of Inclusive Teaching

Irrespective of the curriculum , concepts or content, to serve our students requires faculty that are well versed in inclusive teaching if we are to meet the challenges facing not only our discipline, but also science in general. Few faculty seem aware of the problems that stereotype threat in our classes present nor are trained in ways to avoid putting students at a disadvantage in our classrooms despite a number of studies on this topic specifically in science education (*83–87*). As a start to informing and discussing this issue amongst faculty, perhaps all faculty should be required to read "Whistling Vivaldi" (*88*) as part of their summer reading!

Appendix: Based upon, with Expanded Detail, Wright et al. (9) "Essential Concepts and Underlying Theories from Physics, Chemistry, and Mathematics for 'Biochemistry and Molecular Biology' Majors"

Gateway Concepts from Physics

Coulomb's Law

Interaction between charges, the charges, q, may be full, formal charges, +, -, or partial charges, δ+, δ-, and from the equation below, the force between them will be attractive, opposite charges, or repulsive, like charges. The value of F being either negative, for opposite charges, or positive, for like charges. The separation between the charges is represented by r.

$$F = \frac{\mathrm{k} q_1 q_2}{r^2}$$

Coulomb's law is a vector equation and includes the fact that the force acts along the line joining the charges.

Particularly in a biological setting, you have to consider what is between the charges: with more polar compounds in effect shielding the charges and decreasing the force between them. This is represented by the dielectric constant, D, of the medium. In a biological setting the dielectric constant ranges from 80 for water to an estimated 4-8 in the hydrophobic interior of a protein, and hence has a significant effect on the force between two charges. Where the dielectric constant must be taken into account, Coulomb's Law is represented by:

$$F = \frac{\mathrm{k} q_1 q_2}{D r^2}$$

Energy and Stability

Steric energy of a molecule arises from specific interactions within the molecule. These interactions include the stretching or compressing of bonds beyond their equilibrium lengths and angles, torsional effects of twisting about single bonds, the Van der Waals attractions or repulsions of atoms that come close together, and the electrostatic interactions between partial charges in a molecule due to polar bonds

$$E_{\text{steric energy}} = E_{\text{str}} + E_{\text{bend}} + E_{\text{str-bend}} + E_{\text{oop}} + E_{\text{tor}} + E_{\text{VdW}} + E_{\text{qq}}$$

Bond stretching, bending, stretch-bend, out of plane, and torsion interactions are bonded interactions because the atoms involved must be directly bonded or bonded to a common atom. The Van der Waals and electrostatic (qq) interactions are between non-bonded atoms.

As a result, in general for a molecule, High Energy = Low Stability.

Newton's Laws of Motion

First Law: an object will remain at rest or in uniform motion in a straight line unless acted upon by an external force.

Second Law: F=ma

Third Law: for every external force that acts on an object, there is a force of equal magnitude but opposite direction which acts back on the object which exerted that external force.

Friction

For a moving object, frictional resistance is usually proportional to the "normal force" and designated by N.(the force perpendicular or "normal" to the surfaces). Friction is independent of the area of contact and the coefficient of static friction is slightly greater than that of kinetic friction. In general, kinetic friction is independent of velocity. Friction is proportional to the roughness of the surfaces in contact.

The frictional resistance force may then be written: $f_{friction} = \mu N$

μ_k = coefficient of kinetic friction

μ_s = coefficient of static friction

Hooke's Law

An elastic object, such as a spring, at equilibrium has a defined length. If the spring is either stretched or compressed , the change in length is called its extension and has either a +ve value (stretched) or a -ve value, (compressed). The extension of an elastic object is directly proportional to the force (F) applied to it, related by Hooke's Law

$$F = k.e$$

Where F is the force in Newtons, k is the Spring Constant in N/meter,(the greater the value of k, the stiffer the spring), and e is the extension (compression) in meters.

The Potential Energy stored in a spring, Uel(x) = ½ k x2, (where x = e). For a Harmonic Oscillator, the frequency of the oscillation, f, is related to k by the relationship

$$F = \pi/2 \quad k/m$$

And the wavenumber, υ is πc/2 k/μ

Where $\mu = m_1m_2/(m_1+m_2)$, and c is the speed of light.

Stronger bonds have larger values of k, and give faster vibrations. Bonds to lighter atoms have faster vibrations than bonds to heavy atoms.

Concept of Diffusion

Diffusion is the thermal motion of all (liquid and gas) molecules at temperatures above absolute zero. Diffusion rate is a function of only temperature, and is not affected by concentration. Brownian motion is observed in molecules that are so large that they are not driven by their own thermal energy but by collisions with solvent particles. They move at random because they frequently collide. Molecular diffusion is relevant only on length scales between nanometer and millimeter. On larger length scales, transport in liquids and gases is normally due to another transport phenomenon, convection.

Free Energy, Enthalpy, and Entropy

Spontaneous changes are ones in which the free energy (G) of a system decreases (ΔG is negative). Heat energy is also called enthalpy (H). When heat is released, the change in the enthalpy for the system that is releasing the heat decreases, whereas when heat is absorbed, the change in the enthalpy increases. While a decrease in the enthalpy makes a process more spontaneous (favorable), the change in enthalpy alone cannot be used to predict whether an overall change is spontaneous. There is another factor that must be considered and that is the entropy (S). Entropy is a measure of disorder; when a system becomes more disordered, the change in entropy is positive. When a change in entropy is positive, it makes the change more spontaneous (favorable). In general reactions are favorable if $\Delta H° < 0$ and $\Delta S° > 0$, or unfavorable if $\Delta H° > 0$ and $\Delta S° < 0$,

$$\Delta G^o = \Delta H^o - T\Delta S^o$$

It is critical to appreciate the difference between **ΔG°** and **ΔG. ΔG°** indicates standard conditions and M concentrations of reactants and products at equilibrium since **ΔG°** = -RTLog$_n$K$_{equilibrium}$. **ΔG° tells you the Equilibrium position attained if the reaction occurs.ΔG° does not tell you whether the reaction will occur, or in which direction the reaction will proceed.**

ΔG, on the other hand, is the free energy under the conditions at hand, with

$$\Delta G = -RTLog_n Q$$

Where Q, the so-called Reaction Quotient = [Products]/[Reactants]

ΔG° and **ΔG are related by the equation**

$$\Delta G = \Delta G^o + R\,T\ln Q.$$

If $K_{equilibrium} > Q$, the reaction will proceed forward, converting reactants into products. If $K_{equilibrium} < Q$, the reaction will proceed in the reverse direction, converting products into reactants. If $Q = K_{equilibrium}$ then the system is already at equilibrium and $\Delta G = 0$.

Neither **ΔG nor ΔG° tell you anything about how fast the reaction will proceed. How fast the reaction proceeds requires knowledge of the Activation Energy of the reaction.**

Gateway Concepts of Structure from Chemistry

The structure (both in terms of through bond connectivity (covalent bonds) and through space interactions (non-covalent interactions, both favorable and repulsive)) of a molecule determine its dynamic properties and reactivity (chemical and physical): i.e. its function. 5 gateway concepts of bonding and interactions lay the foundation for understanding protein structure function relationships and the structure, activity and regulation of enzymes.

1: Core Concepts of Covalent Bonds and Polarity

For small molecules (1 or a limited number of "central" atoms), 3-Dimensional structures are determined by bond angles and lengths and geometric considerations involving both bonding and non-bonding (lone pair) electrons based upon Coulombic repulsion of electron density [Lewis Dot Diagrams and VSEPR].

Combinations of atomic orbitals (usually s, p or hybridized in biochemical systems) to give bonding can be described by the appropriate Schrodinger equations [Wave-functions]and the Born-Oppenheimer approximation [scheme] or valence bond theory[scheme] to give bonding and antibonding molecular orbitals [energy levels] and can be used to construct a molecular potential energy surface.

2: Bond Rotations and Vibrations

The chemical bond between 2 atoms vibrates as a harmonic oscillator to allow bond stretching. [diagram]. Such stretching may be symmetric or asymmetric in a molecule with a central atom. In such molecules bending motions may also occur [Energy of a Molecule].

The time scale of such bond vibrations is on the order of 10^{-13}-10^{-14} seconds. As a result of the high energy cost of deforming bond lengths and angles, such vibrations are usually of small amplitude.

Rotations about single covalent bonds can occur with energy barriers to rotation on the order of 10-12kJ/mole in simple molecules without steric hindrance, and time scales on the order to 5 x 10^{-10} seconds.

3: Hydrogen Bonds and Other Noncovalent Interactions

A variety of non-covalent interactions are based upon Coulombic interactions between opposite (attraction) or like (repulsion) charges involving either full (ionic) or partial (Van der Waals or Hydrogen Bond) charges rather than sharing of electrons as in covalent bonds.

Such interactions can involve Charge-Dipole, Dipole-Dipole, or Induced Dipole interactions and the magnitude of the interaction energy, as a result of Coulomb's Law, shows a dependence on both distance and the local dielectric environment. Coulombic interactions can be attractive or repulsive and both play critical roles in molecular structure and dynamics.

Hydrogen bonds can be classified as Strong (2.2-2.5Å, ΔG = 40-14kcal/mol), Moderate (2.5-3.2Å, ΔG = 15-4kcal/mol) and weak (3.2-4.0Å, ΔG < 4kcal/mol) with the strength of the bond progressively decreasing as the angle between the involved atoms deviates from 180°. Hydrogen Bonds may be bifurcated. There appears to be a potential "covalent" contribution (sharing of electron density) in some strong Hydrogen Bonds.[Comparison to Covalent and Ionic Bond strengths].

The force between two atoms in non-covalent interactions can be described by the Lennard-Jones Potential involving the equilibrium distance of the two atoms (the Van der Waals radius), the attractive interactions, and the repulsive forces resulting from overlapping atomic orbitals.

4: The Hydrophobic Effect

Non-polar molecules, as a result of their local dielectric constant, structure a cage of polar solvent molecules around them, resulting in a decrease in the entropy of the system.

The hydrophobic effect is the coming together of 2 or more non-polar molecules in a high dielectric solvent with a concomitant decrease in the overall structuring of solvent molecules and an increase in the entropy of the system.

The magnitude of the hydrophobic effect is proportional to the number of C-H bonds in the molecule excluded from the polar solvent by the interaction.

The ΔG for the interaction of two non-polar molecules comes predominantly from the entropy increase in the polar solvent molecules of the system: $\Delta G = \Delta H - T\Delta S$, with ΔS being large and positive overall with the resultant ΔG being negative.

5: Dynamic Aspects of Molecular Structure

As a result of the properties of bonds and interactions a molecule is not a static structure.

Bond rotations and vibrations combined with inter-molecular non-covalent interactions (attractive and repulsive) allow a potential energy surface to be calculated (approximated for large molecules). The potential energy of a molecule (which is the sum of all of the possible bonded and non-bonded interactions) determines the "structure" of a molecule, which can be described in terms of Potential Energy minima, the local equilibrium structures, and saddle points which represent transition states from one local equilibrium structure to another.

Molecular motion can be described in terms of small amplitude motions (within an energy well on the surface) or large amplitude (between energy wells on the surface).

An ensemble of chemically identical molecules will be distributed between accessible (depends upon the temperature of the system) potential energy minima on the surface proportional to the depths of the minima, and can freely interchange between these local energy minima.

Gateway Concepts of Reactions (and Interactions) from Chemistry

Enzymes are biological catalysts that enable cells to control the wide variety of chemical reactions that continuously occur in a cell. Enzymes enable these processes to occur at ambient temperatures, with the requisite specificity, and unlike chemical catalysts, exhibit the phenomenon of saturability. The reactions catalyzed by enzymes often have mechanisms for regulation of the rates of the reactions. While many enzymes are proteins, some RNA molecules also exhibit enzymatic activity and are termed "catalytic RNA." In all cases, the interactions of enzymes with their substrates, products, and, if appropriate, regulatory molecules are governed by the same foundational concepts that govern chemical reactions in general. Presented here are 5 "gateway" concepts necessary to understand the action of enzymes from a chemical perspective.

1: Collision Theory

Reactions require collisions between molecules.

Not all collisions can lead to product formation because of necessary energy conditions, orientation or steric factors.

Only collisions with the correct orientation and with sufficient energy to overcome the activation energy of the reaction will be successful.

Collision Theory predicts the concentration dependence of a reaction.

Collision Theory predicts the temperature dependence of a reaction.

2: Transition State Theory

Reactions proceed through formation of an "activated complex" that lies at a saddle point on the Potential Energy Surface between reactants and products. This activated complex is the Transition State of the reaction.

The transition state for the reaction is in Quasi-Equilibrium with the reactants and products of the reaction.

The transition state can convert to products and kinetic theory allows calculation of the rate of this process.

Transition State Theory allows for the calculation of the standard enthalpy of activation ($\Delta H^{\#}$), the standard entropy of activation ($\Delta S^{\#}$), and the free energy of activation ($\Delta G^{\#}$) from experimental data using the Eyring Equation (which resembles the Arrhenius Equation) relating the reaction rate to the temperature.

3: Rate Laws, Steady States, and Equilibria

Rate laws for a reaction (which are usually experimentally determined) describe the dependence of the rate of the reaction on either concentration of the reactant(s) (Differential Rate Law) or the time of the reaction with a fixed starting concentration (Integrated Rate Law)

In Differential Rate Laws, depending upon the order of the reaction, the rate is proportional to the concentration of the reacting species and on a rate constant for the process.

The Integrated Rate Law relates the concentration of reactant (or product) to the time of the reaction and the initial concentration of reactant.

The format of rate laws (differential or integral) depends on the Order of the Reaction.

In a Steady State, the concentrations([x]) of the components of a system do not change over a period of time (t) and can be represented by $\delta[x]/dt = 0$.

While a steady state is not necessarily at Equilibrium, an equilibrium, by definition, is a steady state and defined by an equilibrium constant, $K_{EQ} = [Products]/[Reactants]$.

As a result of rate laws, the Equilibrium Constant for a reversible reaction is related to the individual rate constants for the forward and reverse reactions ($K_{EQ} = k_f/k_r$) and the energy difference between reactants and products($\Delta G° = -RTlnK_{EQ}$).

4: The Effects of Temperature

Increased temperature, in general, leads to increased reaction rates as a result of increased collision frequency (small effect-frequency of collisions is proportional to square root of K) and an increase in the proportion of the molecules that have sufficient energy to react (large effect due to shift in Maxwell Boltzmann distribution, etc.) when they collide correctly.

Increased reaction rates, reflected in the rate constants for the reaction, may affect forward and reverse reactions differently resulting in equilibrium constant effects of temperature.

In the energy diagram for a reversible reaction, increased temperature in effect "raises" the energy of the reactants while decreased temperature lowers the "energy" of the reactants. Temperature changes have little effect on the energy of the transition state.

The effects of temperature on reaction rates or equilibrium constants are described quantitatively by the Arrhenius and Van't Hoff equations, respectively, and allow the appropriate thermodynamic data to be calculated from the temperature dependence of either rate or equilibrium constants.

As a general rule of thumb, in biological systems, a 10K rise in temperature approximately doubles the rate of a reaction.

5: Structure and Reactivity

Chemical Reactions involve bond breaking or bond making events and involve changes in the electron sharing within or between molecules and are usually discussed in terms of three fundamental concepts: i) nucleophiles and electrophiles, ii) acid-base chemistry, and iii) redox reactions.

Nucleophiles and electrophiles: the electron density of a given molecule determines its reactivity, which can be influenced by the electron density of the molecule with which it is reaction. Nucleophiles are regions of a molecule that are electron rich, while electrophiles are regions that are electron deficient.

Nucleophilicity increases as you increase basicity.- The conjugate base of a compound is always a stronger nucleophile. The most common nucleophiles contain lone pairs or pi bonds (especially with electron donating groups attached), although sigma bonds can be involved in some cases. Substitution reactions often include water as the nucleophile. For leaving groups, the weaker the conjugate base, the better the leaving group. In biochemistry, ATP is often involved to make a good leaving group (). The strength of an electrophile is governed not only by its electron deficiency, but also by steric considerations and the stability of a potential carbocationic intermediate in s_N2 reactions.

Modern concepts of acids and bases are derived from the Arrhenius theory (acids produce hydrogen ions, bases hydroxide ions), and include the Bronsted-Lowery theory (an acid is a proton donor while a base is a proton acceptor) and Lewis theory (an acid is an electron pair acceptor while a base is an electron pair donor).

Acid-base chemistry in the molecular life sciences mostly involves weak acids and bases (only partially ionized in water) where pKa = -log Ka where Ka = ($[A^-][H^+]$)/[HA]. The Henderson-

Hasselbach equation (pH = pKa + log[A^-]/[HA]) can be used to assess the state of ionization of a group at any pH. There is a relationship between weak acidity to structure (the stability of the conjugate base, etc. - eg serine vs cysteine). Changing the local environment (charge environment, polarity of environment, etc.) has an effect on the pKa of a weak acid. The Henderson-Hasselbach equation is also the foundation for understanding buffers and titration curves.

In Redox reactions, oxidation is loss of electrons, while reduction is gain of electrons. In such a reaction you can consider two "half reactions," but you cannot have one half reaction without the other-half reaction. An oxidizing agent gains e^- during reaction and is therefore reduced during reaction, while a reducing agent loses e^- during reaction and is therefore oxidized during reaction. The oxidized form of a molecule is the form of molecule lacking e^- and the reduced form of a molecule is the form of the molecule having e^-.

Oxidation numbers are often used to consider molecules undergoing redox reactions. For atoms in their elemental form, the oxidation number is 0. For ions, the oxidation number is equal to their charge. For single hydrogen atoms, the number is usually +1 (but in some cases, it is -1). For oxygen, the number is usually -2. The sum of the oxidation number (ONs) of all the atoms in the molecule or ion is equal to its total charge.

For the general redox reaction (written as a reduction) aA + n e-←→ bB the Nernst equation takes the form:

$$E = E^o - (RT/nF) \log [(A_R)^b / (A_O)^a]$$

Where E is the measured electrode potential, E° is the standard reduction potential, R is the gas constant (8.314 J/mol K), T is temperature in K, n is the stoichiometric number of electrons involved in the process, F is the Faraday constant (96,485 C/mol) and A_R and A_O are the activities of the reduced and oxidized members of the redox pair, respectively.

In considering redox reactions, you need to account for all of the electrons as they transfer from one species to another, and deal with each of the two half-reactions individually.

Overview of Types of Enzyme Chemical Mechanisms:

Six basic types of enzyme activities exist based in large part on the type of chemical reactions they catalyze. As categorized by the Enzyme Commission, these are: 1) Oxidoreductases- involve oxidation/reduction reactions- movement of electrons between molecules, 2) Transferases- mostly substitution reactions (usually with alcohol, amine, or thiol as nucleophile), 3) Hydrolases- mostly substitution with water as nucleophile, 4) Synthases/Lyases- reactions where two molecules are brought together (or broken apart) that is not already class 1 or 3; can be aldol reactions, eliminations, additions, etc., 5) isomerases- where you switch between isomers (constitutional or stereo). Can involve cofactors. Can involve acid/base chemistry or substitution, etc. and 6) Ligases/Synthetases- usually substitution reactions, but need ATP (usually) to make a good leaving group.

Gateway Concepts from Mathematics

Models

Models play important roles in science and come in three types: Physical, Mathematical, and Conceptual and usually involve three components, i) Information input, ii) an Information processor, and iii) Information output (often some type of prediction). Physical and Conceptual models (sometimes referred to as Mental Models) are often qualitative, while Mathematical (and

Statistical) Models are quantitative. All Models have limitations, but are useful in generating avenues to "test" the model, and, as a result, are often changed based upon new evidence. The most useful models are the simplest model that accommodates the available evidence

Randomness and Stochastic Processes

Stochastic vs Deterministic Processes. A stochastic process, X(t) or Xt, is a collection of random variables indexed by time, t. Discrete or continuous time Markov Chains. A process is deterministic if its future is completely determined by its present and past. A Markov chain is a stochastic process, but unlike a general stochastic process, Markov chains must be "memory-less" and the probability of future actions are independent of the preceding steps that gave rise to the current state.

Probability

Probability Models- 3 components: 1] sample space (set whose elements are the "outcomes" or "sample points" 2] class of "events" (all subsets of the sample space) and 3] Probability Measure (assignment of a nonnegative number to each outcome, with the restriction that these numbers must sum to one over the sample space).

The probability of an event is the sum of the probabilities of the outcomes comprising that event.

Deriving Equations

Equations can be developed based upon a theoretical model (e.g. chemical and enzyme kinetics) or on experimental observations (e.g. Coulomb's Law).

Using Equations

Equations describe many processes in the molecular life sciences: linear- $y=mx + c$, hyperbolic- $y=mx/(x+K)$, exponential rise- $y=a(1-e^{-kx})$, exponential decay-$y=ae^{-kx}$

Sigmoidal-$y=y_o+a/(1+e^{-((x-xo)/b)})$ and allow descriptor constants, m, K, k, a, b, etc. to be calculated from experimental data. Equations also allow experimental data to be extrapolated to predict values for the observable, y, for inaccessible values of the independent variable, x.

Populations, Averages, Normal Distributions, and Standard Deviations

Reproducibility and error analysis: average, x = Σxi/n. Sample standard deviation is the square root of Σ(xi-xav)2/(n-1). If you compare two normal distributions and take 95% confidence limits: i.e. the values laying between the 2.5% and 97.5% values, of each distribution and the values do not overlap, there is only 2.5% of the possible estimates of the higher number that could, in a normal distribution, fall into the upper echelons of the normal distribution of the lower number: the numbers would be said to differ at the level of the 95% confidence limits, or at a p value of 0.025.

Linear Regression and Residuals

Least squares analysis involves making an initial guess to the values of the parameters of the equation being fit and calculating using these initial guesses the values of y for the chosen values of x. The difference between theoretical and experimental data points is the "residual" and is negative or positive depending upon whether the calculated value is bigger or smaller than the actual experimental value. The residuals are squared and summed. The sum of the squares of the residuals is hence an estimate of the fit of the line to the data. The parameter estimates are then changed and a sum of squares of the new residuals calculated. The process is repeated until the sum of squares of the residuals is a minimum. The parameters giving the lowest sum of squares of the residuals are the best fit parameters. The residual is the difference between the actual data point and the computed best fit data point and can be negative or positive. The residuals calculated from these best fit parameters can be plotted against the value of x, and a random distribution of residuals indicates the correct equation was used. A pattern in the residuals indicates that a different equation is more appropriate

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