Bridging the Gap

Bridging the Educational Research-Teaching Practice Gap

FOUNDATIONS FOR ASSESSING AND DEVELOPING BIOCHEMISTRY STUDENTS’ VISUAL LITERACY

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External representations (ERs), such as diagrams, animations, and dynamic models are vital tools for communicating and constructing knowledge in biochemistry. To build a meaningful understanding of structure, function, and process, it is essential that students become visually literate by mastering key cognitive skills that are essential for interpreting and visualizing ERs. In this article, first we describe a model of seven factors influencing students’ ability to learn from ERs. Second, we use this model and relevant literature to identify eight cognitive skills central to visual literacy in biochemistry. Third, we present simple examples of tasks as a foundation for designing more sophisticated and complex items for assessing and developing students’ visual literacy. We conclude that visual literacy is fundamental to the development of sound conceptual understanding and it is crucial to develop visual skills in parallel with meaningful learning outcomes in all biochemistry curricula.

Keywords: Visual literacy, developing interpretation and visualization skills, assessment, external representations, meaningful learning.

In two previous “Bridging the Gap” articles [1, 2] we focused on the assessment of various cognitive skills necessary for conceptual understanding. In addition, biochemists require other cognitive skills for visualizing and interpreting the myriad of external representations that communicate our science [3]. We use external representations (ERs) to describe the range of visual tools used to communicate scientific knowledge in the external world (e.g. [4]). ERs can be static or dynamic and include diagrams, pictures, physical models, animations, simulations, multimedia, and virtual realities. In the submicroscopic, abstract world of biochemistry, interpreting ERs is often the key to unlocking a meaningful conceptual understanding of structure, function, and process [3]. However, the ERs that we use can be graphically complex in terms of their constituent symbolic language and therefore difficult for students to interpret. Thus, it is crucial to develop our students’ visual literacy [3] to scaffold our students along the novice to expert continuum [1]. According to Bamford [5], visual literacy encompasses the skills required to read and write visual or symbolic language including the ability to, (i) decode and interpret ERs, (ii) encode and construct meaningful ERs, (iii) visualize objects in the “mind’s eye” and, (iv) comprehend ERs generated by others.

Voet and Voet [6] have pointed out the importance of visual literacy in modern biochemistry in light of an improved ability to visualize and study protein structure and function with modern computer-based technologies (e.g. [7]). Examples of useful educational resources include a java-based visualization environment constructed by Bottomley et al. [8] and a Jmol resource for interactive molecular visualization by Herráez [9]. More recently, Hodis and Sussman [10] have developed an open resource (wiki) called Proteopedia that links descriptive text to manipulatable 3-D structures. Although numerous other visualization resources continue to enter the biochemistry education scene, only limited empirical research exists on students’ interpretation and visualization of ERs in our science. Recent studies include students’ interpretation of, and learning with, physical models (e.g. [11, 12]), static pictures (e.g. [13, 14]), animations (e.g. [15, 16]), and virtual environments (e.g. [17]). Although the increase in the number of studies in the field is encouraging, little attempt has been made to identify the specific cognitive skills associated with expert-level visual literacy, let alone the assessment thereof. Avgerinou and Ericson [18] support the urgent need to explicitly distill such skills and surmise that, “higher order visual literacy skills do not develop unless they are identified and taught” (p. 288).
To induce “bridging the gap” between empirical science education research on visual literacy and its actual application to improving learning and teaching in biochemistry, this article addresses the following three questions:

- What factors affect students' ability to interpret and visualize ERs in biochemistry?
- What cognitive skills are central to the visual literacy of expert biochemists?
- What simple examples of tasks can offer points of departure for assessing and developing students' visual literacy in biochemistry?

**FACTORS AFFECTING STUDENTS’ ABILITY TO INTERPRET ERs**

Our research has modeled at least seven factors that affect students' ability to interpret, visualize, and learn from ERs in biotechnology [4]. These factors may be important to consider when investigating the notion of an expert-level visual literacy in biochemistry. The factors of the model are expressed in the form of a Venn diagram presented in Fig. 1.

The conceptual factor (C) of the model represents a student's conceptual knowledge, of relevance to an ER, whereas the reasoning factor (R) encapsulates the repertoire of cognitive skills that a student might utilize when interpreting and visualizing an ER. The representation mode factor (M) characterizes the actual nature of the ER, including the symbolic language that composes the ER. As shown in Fig. 1, these three factors are interdependent in that students cannot use their cognitive skills to do any reasoning (sense-making) without something to reason with, namely the ER (Factor R-M) and/or their own conceptual knowledge (Factor R-C). Thus, R-M represents a student's ability to decode the symbolism making up the ER, whereas R-C represents the ability to employ the appropriate conceptual knowledge necessary for interpreting the ER. The (C-M) interactive factor represents the scientific (propositional) knowledge represented by the ER and its constituent symbolism. Finally, the (C-R-M) interactive factor encompasses a student’s simultaneous engagement of all the factors essential for the successful interpretation of an ER [4].

This model has important implications for biochemistry learning and teaching. First, it prompts instructors to realize that a certain minimum amount of prior conceptual knowledge (C) is indispensable to the interpretation of an ER. If such knowledge is lacking, or unsound due to alternative conceptions, then the student will compromise their ability to learn from the ER and successfully acquire the knowledge it represents (C-M). Thus, it is important that instructors establish the state of students’ prior knowledge before they expose them to particular ERs. Second, the model reminds us that learning from an ER is highly dependent on the nature and quality of the ER and its constituent symbolism (M) in effectively representing the scientific knowledge that it intends to represent (C-M). Here, an important message for instructors is to evaluate the soundness of an ER before exposing students to it. Indeed, a major area of visualization research consists of identifying what criteria are important when designing pedagogically effective ERs (see [19]). Furthermore, even if the ER is sound, instructors should also confirm whether it is intelligible to students and, if not, explicitly explain the meaning of the constituent symbolism as well as the limitations of the ER. Third, the model reminds instructors that having the necessary prior conceptual knowledge (C) and a highly effective ER (M) is still insufficient if students’ lack the cognitive skills (R) to both engage the appropriate conceptual knowledge necessary for interpreting the ER (R-C), and to decode the symbolic language used in the ER (R-M). Thus, it is of utmost importance for instructors to develop such cognitive skill competence (R) in their students, a fundamental goal that is the focus of the next section.

**IDENTIFICATION AND ASSESSMENT OF COGNITIVE SKILLS CENTRAL TO EXPERT VISUAL LITERACY**

In this section, we address the second and third questions raised in this article namely, what cognitive skills (R-C and R-M factors, Fig. 1) are central to the visual literacy of expert biochemists, and what tasks can assess and develop students' visual literacy in biochemistry?

A synthesis of literature from the past 10 years has led to the identification of eight visual skills (Table I) associated with the notion of an expert visual literacy. Although some of the skills overlap in terms of objectives, we have purposely kept them separate so that instructors can more easily develop and assess each individual competency in their students. In so doing, one should recognize that no task can exclusively assess a single skill. As will be shown in this article, all tasks require students to simultaneously engage more than one of the skills listed in Table I, as well as several other cognitive skills, discussed elsewhere (See [1, 2]). In the interests of clarity, we have purposely pitched the tasks presented in this article at an introductory biochemistry level, with the idea that instructors could use them as a basis for designing more sophisticated tasks for higher educational levels and different biochemistry contexts. All the tasks were trialed in an introductory course on protein structure and function. Student responses to each task were screened to establish whether the particu-
lar visual skill was being tested. Preliminary findings suggest that our goals are being achieved although an empirical educational research study is required to fully validate the tasks. In this regard, we are currently conducting clinical interviews to meta-tag these and several other more sophisticated questions for assessing and developing visual skill competence in students. Such studies are beyond the scope of the present article.

**Decode the Symbolic Language Composing an ER**

All ERs are composed of symbolic language that needs decoding during the interpretation of an ER (Table I). In biochemistry, ERs can be particularly challenging for students to decode because of the great diversity of often idiosyncratic symbolism that may look aesthetically pleasing to viewers but does not always convey the intended scientific meaning [3]. For example, the same concept may be represented by several different symbols or, one symbol might be used to represent several different concepts (e.g. [13]). Consequently, there is extensive evidence for student difficulties with the decoding of the symbolism in ERs (Table I). For example, some students misinterpret ERs by focusing only on certain salient markings (e.g. brightly color symbols) at the exclusion of others (e.g. [14]). Furthermore, where ERs are part of assessment tasks, a poorly designed ER, and not necessarily student conceptual knowledge, may be the cause of incorrect responses [41]. In the case of animations, the interpretation of moving graphical markings within restricted times can also create cognitive difficulties for students [34].

Despite these problems, many instructors make little effort to specifically explain an ER and its symbolism to students as they (mistakenly) assume that, because the ER is clear to them, the same will automatically hold for their students [19]. Thus, it is important to develop students’ skills for decoding ERs [25, 41]. One way to achieve this is to give students tasks that require them to use symbolism “keys” as a tool for decoding ERs. For example, the Protein Chart of Garratt and Orengo [42] can be used to interpret ribbon symbolism representing major domains (e.g. β-barrels), motifs (e.g. leucine zipper), and oligomeric proteins (e.g. proteasome) and to link such structures to cell functions. Another way to develop students’ symbolic language and skills is to give them extensive practice at answering formative assessment tasks that require them to decode symbolism, as well as combinations of symbolism, inherent in ERs from a wide range of topic areas. Qu. 1 is a simple example of such a task. Note that decoding a ball-and-stick representation does not only involve a surface-level perceptual process (factor R-M), but also the engagement of conceptual knowledge represented by the symbolism (factor R-C) [4].

**Qu. 1:** Consider the peptide represented in Fig. 2.

(a) Describe what the different “balls” and “sticks” represent in terms of peptide structure.

(b) Label the N- and C- termini of the peptide.

(c) How many peptide bonds are present in the structure?

**Evaluate the Power, Limitations, and Quality of an ER**

Closely related to the decoding of symbolism is the importance of developing students’ ability to evaluate the representational power, limitations and overall quality of ERs (Table I). Representational power is about how successfully a particular ER achieves its intended goal(s) (factor C-M), whether this be helping to develop a mental model of a concept, structure or process, or as a tool for solving a problem. As a first step in evaluating the power of the ER, it is crucial to ascertain what the goals of the ER are by deducing the limitations of the ER in terms of what parts of the phenomenon are, and are not, represented by the ER. Such limitations are not necessarily a weakness of the ER as the real power of a model is often (but not always) in its simplicity rather than its complexity (for example, Fig. 2 only depicts selected features of peptide structure). Thus, the aim of ER designers should be to develop multiple representations (Table I) of a phenomenon with each representation depicting selected features of the entire phenomenon in as clear a manner as feasible. Having established the goals of an ER, the

**FIG. 2.** ER depicting a peptide in a conventional “ball-and-stick” format. Display generated with Viewer-Lite 5.0, Accelrys Software Inc.
second crucial step in determining the power of an ER is to evaluate how accurately and effectively the ER, and its constituent symbolism, conveys the intended scientific knowledge so that these goals are achieved. Indeed, as already discussed, symbolism can often be confusing and misleading and significantly affect the overall quality of the ER. Hence, it is important to develop students’ representational competence [43] by giving them practice at answering assessment tasks that require critical evaluation of the quality of (“good” and “bad”) ERs. Qu. 2 is a simple example of such a task. Other more sophisticated tasks could of course involve the use of molecular viewing software as well as animated and stereo tools.

Qu. 2: Consider the ER in Fig. 2 and list which structural features of the peptide:

(a) Are represented by the ER.
(b) Are not represented by the ER.
(c) Comment on how clearly you think the ER and its constituent symbolism, represents the structure of the peptide.

Interpret and Use an ER to Solve a Problem

Interpretation of an ER can only occur once all the symbolic language composing the ER has been decoded (R-M). Once this has occurred, the individual can construct a mental model of the ER as an integrated whole and can interpret it by linking it (R-C) to the conceptual knowledge it represents (C-M). Having interpreted the ER, the individual is then in a position to use the ER for a range of tasks including, solving a (novel) problem, making a prediction, or constructing new conceptual knowledge (Table I). Qu. 3 is a simple example of a task that uses an ER to assess and promote the development of problem-solving skills in biochemistry.

Qu. 3: Consider the peptide represented in Fig. 2:

(a) Identify the amino acid residues from the N- to the C-terminus.
(b) How many groups would be protonated at a pH of 7.0?
(c) How many double bonds are there in this peptide? Identify them.
(d) Which residues in the peptide can display hydrophilic properties? Explain why.

Spatially Manipulate an ER to Interpret and Explain a Concept

Much chemistry education research has shown that spatial visualization skills are essential for interpreting 2-D ERs that portray 3-D objects, and that students show extensive difficulties in performing these processes [41]. In biochemistry, only a limited number of educational studies have been done on spatial visualization skills (e.g. [26]) despite the diversity of complex biomolecules that require visualization via various computer and physical ERs. In addition, spatial skills are required for interpreting, inter alia, animations of cellular processes, electron micrographs of cellular structures, and Cartesian graphs [4].

Tuckey and Selvaratnam [44] identified several skills as being important for the visualization of 3-D molecules from 2-D ERs. These include the ability to decode symbolic depth cues, understand the spatial relationships (width, depth, and height) represented in the 2-D ER, mentally manipulate an ER in the “mind’s eye,” and visualize its transformation. Assessment tasks that make use of modeling software offer the opportunity to develop such skills in our students. Moreover, modern virtual reality environments that incorporate haptic feedback (see [17]) provide a unique alternative for developing spatial skills through the sense of touch. Related to this, Roberts et al. [12] have shown that students can develop spatial skills through the tactile manipulation of physical models, while Harris et al. [26] have shown that a combination of physical and computer-generated ERs can achieve this goal. Importantly, a recent article [7] on macromolecular visualization points out that research is only starting to establish how best to use physical models in structural biology education. As a further step in this direction, albeit in a simple form, Qu. 4 is an example of a task that could be used to develop students’ various spatial skills including, depth perception (Qu. 4a), the visualization of the relative configuration of atoms (Qu. 4b), and the mental rotation of molecules (Qu. 4c). Note that such tasks could of course be extended for use within more sophisticated dynamic modeling environments.

Qu. 4: Consider the peptide represented in Fig. 2:

(a) Which one of the oxygen atoms would be closer to you in the present orientation?
(b) Identify whether each of the two peptide bonds is in cis or trans configuration.
(c) Sketch what the peptide would look like after a 180° rotation about the y-axis.

Construct an ER to Explain a Concept or Solve a Problem

Biochemists make extensive use of ER-construction as a problem-solving tool (Table I) to capture a research method overview (e.g. as a flow diagram), relate scientific ideas (e.g. as a concept map), summarize research findings (e.g. as a graph), illustrate mechanisms of cellular regulatory processes (e.g. as an animation), and model 3-D structures. In addition, biochemists might modify or manipulate an ER to, for example, predict what affect an activator or inhibitor might have on the bioactivity of a protein. Thus it is important to develop our students’ ability to construct, modify, and use their own ERs as part of their practice as a biochemist. To achieve this, students should receive extensive opportunities to perform some of the above-mentioned activities. In addition, simple hand-drawing tasks, or exercises requiring the construction of physical models of biomolecules using various materials (see [23, 24]) are ways of developing this competence. An exciting innovation that could also promote ER construction skills is the online protein structure game called Foldit [45]. Foldit requires participants to use various visual skills to fold a ribbon representation of a random coil into its most stable conformation.
Qu. 5 is an example of a simple task that could also be used to develop ER-construction skills, as well as other visual skills (Table I), ranging from decoding (Qu. 5a; Factor R-M) through to ER interpretation (Qu. 5b and 5c) during which adequate conceptual knowledge needs to be engaged (Factor R-C).

Qu. 5: Examine the following representation of a polypeptide sequence:


(a) Use a sketch to predict how this peptide might fold so that the three indicated amino acids are brought into close proximity.
(b) Suggest what type of secondary structure might result from the folding. Explain why.
(c) Suggest what effect(s) could lead to an interaction between the three amino acid residues.

Translate Horizontally Across Multiple ERs of a Concept

It is common practice in the submicroscopic world of biochemistry to use different ERs to represent the same phenomenon or different features of a phenomenon [3]. For example, the concept of enzyme-substrate interaction can be represented by a wide range of different ER modes, including abstract (e.g. Michaelis-Menten formula), symbolic (e.g. chemical equation), graphical (e.g. Michaelis-Menten plot), stylized (e.g. animation of enzyme-substrate binding), and realistic modes (a crystal structure). To develop an integrated understanding of this concept, students would need to “move” or translate across these different ERs, including decoding the different symbolism in each ER and linking the relationships between each ER [46]. Schönborn and Bögeholz [30] have built on the idea of translation in a biology context by defining a horizontal translation, which deals with interpreting ERs that represent a phenomenon at the same level of biological organization, whether it be at the macro-, micro- or molecular level. Qu. 6 is an example of a simple task aimed at developing students’ horizontal translation skills, in this case involving ERs that all depict the molecular level of biological organization (Fig. 3). In this example, translating across all three ERs facilitates the development of a more complete mental model of the structure of the subunit (Qu. 6). Clearly, students will also make use of other skills presented in Table I during this process.

Qu. 6: Consider the left, central, and right ER in Fig. 3 in which each represents different structural features of one beta subunit of human carbonmonoxy hemoglobin. Interpret each of the three ERs and compare them with respect to what they do, and do not represent in terms of the various structural features of hemoglobin.

Translate Vertically Between ERs that Depict Different Levels of Organization and Complexity

All biochemists require the skills to translate vertically “between” levels of biological organization and

Fig. 3. Five ERs that represent different structural components of human carbonmonoxy hemoglobin at 2.7 Å resolutions. The green and blue ribbon representations respectively depict one alpha and one beta chain of the protein (Protein Data Bank ID: 1HCO). Display generated with Viewer-Lite 5.0, Accelrys Software Inc.
complexity [30]. For example, in the case of a biological tissue, it might be necessary to translate between ERs that represent the visible and tangible macro-level, the microscopic level, as well as the molecular level of biological organization [35]. The “distance” of vertical translation required may not always involve a complete macro-micro-molecular transition but could also comprise smaller distances between levels of complexity [30]. For example, Qu. 7 requires students to remain within a molecular domain but to still translate between different levels of complexity.

Various studies have shown that students have difficulties developing the vertical translation skills that characterize expert-level visualization (e.g. [32, 33]). Thus, practice in doing tasks, such as Qu. 7, that explicitly test such skills could improve student competence in this area. In this example, translating vertically between the three ERs allows students to gain a greater appreciation of the additive effect of “moving” through increasing levels of biological complexity.

Qu. 7: Consider the top, central, and bottom ERs in Fig. 3 representing various structural features of human carbonmonoxy hemoglobin. Interpret the three ERs and compare them with respect to the different levels of complexity that they represent.

Visualize Orders of Magnitude, Relative Size, and Scale

Visualizing orders of magnitude and scale is related to vertical translation processes since the latter often includes grasping the absolute and relative size of organs, cells, organelles, and biomolecules. However, competence in the former may achieve much more since it also enables the visualization of the relative quantity of a wide range of biostructures and parameters of relevance to living systems. These could include the approximate number of mitochondria or nuclei in different cell types, the typical concentrations of biomolecules necessary to regulate metabolic systems or to sustain life without reaching toxic levels, as well as the typical magnitude of kinetic constants (e.g. $K_m$, $V_{max}$) and thermodynamic values (e.g. Gibbs energy, redox potentials) that would be realistic in a living system. Visual skills are also required for interpreting log scales used in graphical representations of assays, while the properties of many substances (e.g. enzymes) in living systems change as the scale of parameters such as pH and temperature change. Finally, understanding nanotechnology also depends heavily on skills for visualizing scale (see [22, 37]) while in biology, scale is considered a “threshold” concept in that it is seen as an essential prerequisite for mastering other concepts [36]. Qu. 8 is an example of a simple task that could develop and assess this competency in students.

Qu. 8: Arrange the following structures in order of decreasing size and match each of them with their approximate diameter:

- Proteasome, glucose molecule, red blood cell, water molecule, mitochondrion, ribosome, hemoglobin molecule, typical bacterium, DNA double helix, typical virus
- Diameters: 7 μm, 1–3 μm, 0.5–1.0 μm, 80 nm, 25 nm, 11–15 nm, 6.4 nm, 2.4 nm, 1 nm, and 0.3 nm.

CONCLUDING REMARKS

The eight skills discussed in this article should not be viewed as a complete set of competencies required for optimal visual literacy as numerous other (and often complementary) cognitive skills may influence the visualization process (e.g. [1, 2, 35]). However, by developing competence in these skills, we believe that students will go a long way toward optimizing their ability to interpret and use ERs as effective knowledge-building and communication tools. Clearly, although the success of this endeavor will depend heavily on the nature of the formative and summative assessment tasks [47] that instructors design to respectively develop and grade each skill competence. In this regard, this article provides examples of simple tasks for the assessment of each visual skill that instructors could use as a foundation for the development of more sophisticated tasks. Unfortunately, educators often place little emphasis on actively teaching the skills necessary for interpreting and visualizing ERs [18]. Since visual literacy is fundamental to the development of sound conceptual understanding, a central pedagogical goal of all biochemistry instructors should be to teach and assess students’ visual skills in parallel with the development of all learning outcomes.

- In summary, the main messages conveyed in this article are as follows:
  - Ensure that the ER is an accurate and sound representation of the intended knowledge (C-M);
  - Confirm whether the ER is clear and intelligible to students; if not, explain the ER and its limitations;
  - Ensure that students have the appropriate conceptual knowledge to interpret the ER;
  - Check which of the three factors- soundness of an ER (M), prior conceptual knowledge (C), or cognitive skill competence (R) are limiting, if students show difficulties interpreting the ER, and take appropriate action;
  - Check whether students’ reasoning (R) difficulties are due to inappropriate decoding of the symbolic language composing the ER (R-M), or to inadequate engagement of their conceptual knowledge of relevance to the ER (R-C), and take appropriate action;
  - Design assessment tasks that aim to specifically assess students’ competence in each of the identified visual skills (Table I). Validate each task by means of student interviews to ensure that they are actually assessing the particular visual skill;
  - Use the tasks to formatively develop students’ visual literacy during a course, and to summatively assess their attainment of such competencies at the end of the course;
  - Integrate visual literacy development into all courses across the biochemistry curriculum.

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REFERENCES


dents the visual ability of transforming 1-D information into 2-D and/or 3-D representations.

Qu. 1: Each “ball” represents the center of an atom and each “stick” represents the length and orientation of the covalent bond between two atoms. The grey, red, and blue balls represent carbon, oxygen, and nitrogen atoms, respectively. (b) The C-terminus is located at the carboxyl group represented by the only carbon (grey) atom bound to two (red) oxygen atoms. The N-terminus is the amino group represented by the nitrogen (blue) atom joined to a single alpha carbon atom. (c) 2.

Qu. 2: (a) The following are represented—carbon, oxygen, and nitrogen atoms; covalent bonds between atoms; bond angles; peptide bonds; an aromatic ring; amino acid residues; amino acid side chains; the overall spatial configuration of the actual positions of each atom relative to another. (b) The following are not represented—hydrogen atoms; double bonds in the keto- and carboxyl groups and the aromatic ring; the partial double bond character of the peptide bond; hydrogen bonds; partial charges on the atoms; the surface topography and volume occupied by atoms, groups and the whole peptide molecule. (c) The symbolism in the ER clearly represents the structure of the peptide with the exception that double bonds are represented in an identical mode to that of single bonds. By representing only selected features of the peptide, the ER is simpler and less complex and, therefore, clearer, and easier to interpret. However, multiple ERs are required to represent all features of the peptide to build a more realistic and integrated mental model of the peptide.

Qu. 3: (a) Ser-Lys-Tyr. (b) 1 (alpha NH\textsubscript{3}\textsuperscript{+}) + 1 (epsilon NH\textsubscript{3}\textsuperscript{+}) = 2 protonated groups. (c) Two C=O (peptide bonds) + one C-terminal carboxyl + three C=C (Tyr ring) = 6 double bonds. (d) All three residues can show hydrophilic properties: Water can bind via hydrogen bonds to the epsilon NH\textsubscript{3}\textsuperscript{+} of lysine, the alpha NH\textsubscript{3}\textsuperscript{+}, and hydroxyl group of serine, and the alpha carboxyl and hydroxyl group of tyrosine.

Qu. 4: (a) The hydroxy oxygen atom of the tyrosine residue. (b) The peptide bond between Ser and Lys is in cis configuration and the peptide bond between Lys and Tyr is in trans configuration.

Qu. 5: (a) The peptide would most likely fold into an “S” shape β-meander with the flexible P-G-G-P and G-G-G regions forming beta turns. (b) The folding would lead to the formation of anti-parallel beta sheets. (If the chain was to fold into an alpha helix, the three amino acids would not be in close proximity since they are considerably more than four residues apart). (c) Phe, Ile, and Met could interact through the hydrophobic effect, which, by favoring hydrophilic interactions between solvent molecules, leads to hydrophobic clustering.

Qu. 6: Each ER represents structural features of one beta subunit that the other two do not. The wireframe ER on the left depicts the relative atomic coordinates (and corresponding covalent bonds) that define the overall spatial configuration of the subunit. In contrast, the ribbon ER in the center depicts the subunit’s overall conformation or tertiary structure as well as some secondary structure, consisting in this case of α-helices. The ER on the right portrays the molecular volume occupied by the subunit and therefore the size and shape of the structure’s molecular surface (also see [22]).

Qu. 7: The bottom ER depicts the non-protein prosthetic group found in all four subunits of hemoglobin. The ER in the center represents a higher level of complexity by displaying the location of the prosthetic group relative to the overall conformation of the subunit. The top ER adds a further level of complexity by representing how two subunits would be spatially associated to one another and to each of their prosthetic groups, through noncovalent interactions.

Qu. 8: Red blood cell (7 μm), typical bacterium (1–3 μm), mitochondrion (0.5–1.0 μm), typical virus (80 nm), ribosome (25 nm), proteasome (11–15 nm), hemoglobin (6.4 nm), DNA double helix (2.4 nm), glucose molecule (1 nm), and water molecule (0.3 nm).