Conceptual interference in biological education: How jigsaw puzzle/lock and key models of molecular interactions impact understanding evolutionary change.

Michael W. Klymkowsky

The Bioliteracy Project
University of Colorado, Boulder UCB 347
Boulder, CO. 80309

Abstract: A practical goal in science education research is to identify where the teaching of one concept may impact student understanding of other concepts, presented subsequently. How student understanding of specific concepts interact with one another can be either constructive and reinforcing, or destructive and negating. In the course of research on students' conceptual landscapes as part of the biology concept inventory (BCI) construction project (http://bioliteracy.com), we have come upon an interesting example that illustrates this point. The way proteins in general and protein catalysts (enzymes) interact with their substrates is presented can lead to interference with the understanding of the molecular mechanisms by which evolutionary processes produce novel functions. We will illustrate this interaction and suggest approaches that may help address this particular issue, together with preliminary data on whether these interventions are effective.

Introduction: There are a relatively small number of basic concepts that underlie modern biology. Among these are Theory of Evolution, the Cell Theory and what we might call the Materialistic Postulate. The conceptual basics of the theory of evolution have been well described (see for example Mayr, 2002). In its general form, a population will display evolutionary behavior over time if the individuals within it have hereditable variation and an ability to reproduce that exceeds the ability of the environment to sustain. The Cell Theory holds that all living organisms are composed of cells or the product of cells, and that, at least in the modern world, cells are derived from pre-existing cells. It implies a continuity of life from the origin of the first cells to the modern day. Taken together with the various mechanisms by which populations of organisms can become reproductively isolated, and the impacts of local and global

environmental changes on survival and reproductive success, the Cell Theory and the Theory of Evolution explain the diversity and history of life on earth, and make testable predictions about the structure and history of newly discovered organisms. As molecular methods have advanced, particularly with regards the analysis of regulatory systems and genomic organization, it has become apparent that all extant organisms share a common ancestor that lived some billions of years ago.

The complement to evolutionary theory is the application of the materialistic postulate with regards to biological systems. In brief, it assumes that biological systems are based upon molecular interactions, which while complex, are variants of the interactions found in non-living systems and do not involve any "suprachemical" vitalistic forces. Molecules act upon one another by physical juxtaposition, the specificity of these interactions is based on surface-surface interactions, which involve van der Waals and ionic interactions, e.g. hydrogen bonding and ionic attraction and repulsion. Because most biological systems and molecules occur in an aqueous environment, the chemical properties of water have a particularly important and global impact on biological interactions. For example, the variable affinity of parts of biological molecules for water molecules leads to the "hydrophobic effect", which underlies and is the major determinant of the structure of membranes, proteins, nucleic acids, and other biological components.

A central feature of Darwinian evolution, in molecular terms, is ability of random hereditable changes, mostly due to changes in DNA sequence (mutations), to lead to both deleterious and beneficial changes, in terms of an organism's reproductive success. It is a basic postulate of intelligent design creationists that mutations are uniformly deleterious and that their accumulation cannot lead to novel and complex structures and processes. While the falsity of this premise can be readily demonstrated, through both *in vitro* (e.g. Dobzhansky, 1970; Woods et al., 2006) and *in silico* experiments (see e.g. Lenski et al., 2003; Yedid and Bell, 2002), it is worthwhile to examine whether specific approaches to teaching specific concepts in biology foster or undermine the understanding of the molecular mechanisms of evolutionary change. We will restrict our discussion of the issue to high school and introductory college biology classes, since

these classes impact the largest population of citizens and most students destined become K-12 teachers.

It is common to see interactions between enzymes and their substrates presented in textbooks, and presumably lectures, in the form of jigsaw puzzles and lock and key analogies (**FIG. 1**). These presentations have one obvious advantage; they explain is a simple and direct manner, with strong connections with students' macroscopic experiences how specific interactions occur. At the same time, they obscure an important feature of molecular interactions: molecular interactions are not "yes or no", "fit or do not fit", but rather vary in terms of affinity. Binding affinity itself is a function of the number and strength of interactions between molecules and the effective force of molecular collisions, which acts to knock bound molecules apart. Ignoring for the moment the effects of entropic interactions and ionic repulsions, all molecules have a weak affinity for one another. The net strength of this affinity depends upon the size of the complementary surface area. It is not that two molecules either fit together or not, but how well – the better and more extensive the fit, the stronger the binding interaction between them.

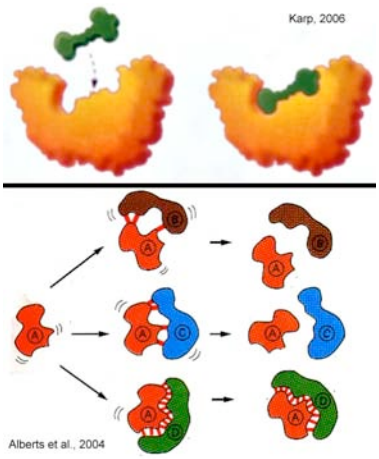


Figure 1: Two figures, modified from Karp (2006) and Alberts et al (2004), show schematics of protein-ligand interactions. Both visualize the interaction as either a perfect fit, or a binary - bound, not bound interaction.

Why is this realization important in terms of understanding evolutionary change? If a student brings a jigsaw/lock & key mindset with them to the study of molecular evolution, they will necessarily assume that every mutation that alters a surface involved in an interaction will disrupt that interactions – jig saw pieces either fit or do not fit, keys either open or do not open a lock. From this perspective, a mutation that alters protein structure even slightly will be expected to destroy, rather than alter, a protein's function and functional interactions. While the student might imagine that the rare mutation may produce a completely new function, this possibility is so unlikely as to be for all intents and purposes impossible. Gradual, that is Darwinian, molecular evolution would be difficult to accept.

The type of mutations studied by genetists generally have drastic effects, primarily because such mutations are selected because they produce easily discernable phenotypes that facilitate experimental analysis. Most mutations, however, have much more subtle effects. If we think about them in the context of enzyme-substrate interactions, they tend to alter the binding affinity or specificity of the interactions a protein can make, rather than abolish a previously existing interaction or establish a brand new one. Such minor mutational changes can alter an enzyme's selectively so that a substrate that previously did not bind effectively can now be bound and reactions involving it catalyzed. Even if inefficient, such altered reactivity can in turn be acted on by selection, and new mutations that further increase substrate selectivity and reactivity can accumulate. This is how new functions appear, through the dialectic between mutation and selection. Each mutation creates a new version of the gene (an allele) that can, in theory at least, influence the reproductive success of the organisms that carry it, and in turn favor other mutational changes. It is the bumpy and inexact nature of molecular interactions that underlies this flexibility, and the possibility of gradual (non-destructive) change.

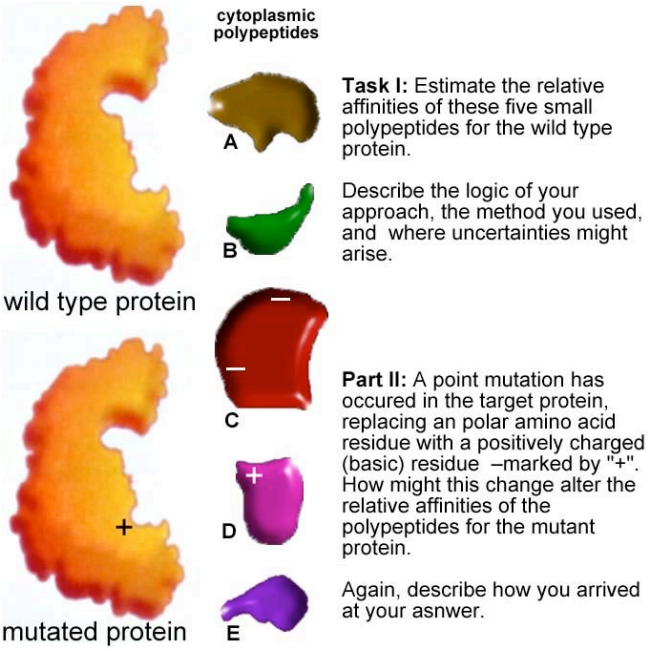
Testing for, and changing the prevalence of, the jigsaw puzzle mind set. One question in the BCI.2006 addresses this issue directly.

Q: How does a molecule bind to its correct partner and avoid "incorrect" interactions?

- ❍ a. The two molecules send signals to each other.
- ❍ b. The molecules have sensors that check for incorrect bindings.
- ❍ c. Correct binding results in lower energy than incorrect binding.
- ❍ d. Correctly bound molecules fit perfectly, like puzzle pieces.

We are currently carrying out reliability testing on this and other BCI questions, and these results, together with the results of qualitative studies will be presented. We already know, however, that many students select "d", whereas "c" more correctly describes the nature of molecular interactions. So how can we encourage students to attain a more nuanced view of molecular interactions? One approach is illustrated by the problem illustrated in figure 2 (below). Here students are presented with a problem

in which they are asked to place a set of polypeptides in order in te Figure 2 g affinity to a target protein. They are then asked to analyze the effect of a mutation that alters the target protein. We are currently testing whether working through this, and related problems, leads to a better grasp of the nature of molecular interactions, in a way that constructively, rather than destructively interferes with an understanding of evolution mechanisms. Interviews with students, and their responses to specific questions in the BCI, will be used to assess the effectiveness of this intervention.



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