Commentary

Inverting Organic and Biochemistry: A Curriculum Tweak That Benefits All

by I. David Reingold

> The need to educate future chemists does not mean that chemistry teachers should pay no attention to the needs and interests of biology students…It is important for chemistry teachers to take into account the interest of all their students, and not pretend that they are all chemistry majors.
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> R. Breslow et al., National Academy of Sciences Report BIO2010: Transforming Undergraduate Education for Future Research Biologists *(1)*

Despite a number of options available, including beginning organic chemistry fall semester freshman year *(2, 3),* spring semester freshman year *(4),* and several more innovative integrated curricula such as those in operation at Illinois Wesleyan and Oberlin, it remains true that the vast majority of U.S. colleges and universities still teach chemistry in a more-or-less standard approach: one year of general chemistry, one year of organic chemistry, and one year of physical chemistry, in that order. Most institutions also require analytical, inorganic, and/or instrumentation courses, and recently, due to new requirements from the ACS Committee on Professional Training *(5),* a biochemistry course, of probably one-semester in the junior year. On top of this there are usually electives and sometimes other requirements.

In this commentary I want to focus on the two courses, organic (full year) and biochemistry. A typical organic chemistry course, as taught from almost any of the many standard textbooks, consists of a brief review of the relevant general chemistry, a discussion of organic structure, and a long list of functional group properties and transformations. These days, instead of memorizing a list of reactions, students are encouraged to understand reactions through mechanisms, using arrow pushing and kinetic and thermodynamic concepts. In addition, students learn to combine reactions in multistep syntheses, and the standard forms of structure identification are discussed. Typically the list of reactions discussed is thorough, since in most departments this is the last organic chemistry course that students are *required* to take, and therefore they try to cover all reactions that are important for chemists to know. I am guessing, but many conversations have confirmed my guess that the cost of this thoroughness is that most courses run out of time before finishing the text, thus leaving out coverage of the final several chapters, including significant discussion of the important biomolecules such as proteins, nucleic acids, and carbohydrates. Of course these topics are covered quite well in the follow-up biochemistry course. Thus all important aspects of organic and biochemistry are covered when both courses are taken. I propose here a simple reorganization of this material that should work to the advantage of all students while retaining the crucial element of covering all important aspects of organic and biochemistry.

The driving force for my proposal is simple: as pointed out by Breslow *(1),* the vast majority of students taking organic chemistry at most institutions are not interested in chemistry *per se*. They are taking chemistry because they have to; about 60–90% of them want to be health professionals or life scientists of some type (including environmental), and the medical schools (or the home departments) require them to take two years of chemistry. Under duress they do so, but they certainly do not intend to take any more chemistry than is required. Therefore we teach them for two years. What do they find in our organic courses? Many topics that are of little interest or use to them, such as the Diels–Alder reaction and ylid chemistry. On the other hand, the aspects of organic chemistry that *are* of intense interest to these students, such as the structure and function of biomolecules and metabolic pathways, are not discussed due to lack of time. I believe this is neither necessary nor desirable.

Proposed Organization

My proposal is simply to reorganize the material so that the majority of the students in the sophomore course (the non-chemists) get what is useful to them, namely, the biological aspects of organic chemistry and the background necessary to understand it, but *not* the esoteric organic chemistry that is of use only to chemists. Further, I propose that the biochemistry taught in the sophomore year not be sequestered into a few weeks at the end of the course, but suffused throughout the course and brought up as often as possible, repeatedly making connections between the organic chemistry being learned and its application to biology. (Perhaps we should rename the sophomore course bioorganic chemistry.) The obvious corollary of my proposal is that the third course in the sequence, taught to juniors, *not* be biochemistry but instead be the rest of organic, now taught to that small group of students who need it. Taking together the bioorganic year and the follow-up organic semester, the same material will be covered as under the present curriculum, but those students who are not chemists will get more chemistry that is useful to them and less that is not.

Note that I am not advocating making the course easier: organic chemistry is and always will be a difficult course for most students. The rigorous process of learning organic chemistry is excellent preparation for medical school and many other professions. But one can learn difficult material that one cares about, or difficult material that is irrelevant. It seems to me that given the choice, the former is clearly preferable.

How, then, do we pull this off? Evaluate the material taught in a standard organic course and identify that material that could be delayed until the third semester without harming the students who will take only two; and also evaluate the material in a standard biochemistry course and figure out where and how to incorporate it into the first two se-

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mesters of the sequence. What follows are my lists. I need to emphasize that my proposal does not depend on the exact content of the lists. Different people will certainly come up with different lists, although discussions thus far have revealed remarkable consensus about most topics.

Features of the Bioorganic Course

Organic Coverage

To make room for the biochemistry that will be incorporated into the course, many aspects of a traditional organic course have to be dropped entirely and other topics treated in less detail than usual. It is important to recognize that this material is not being lost: all chemists *will* see all topics eventually—but it is not necessary that they do so *now*. Further, it is not necessary that the non-chemists see some things at all. See List 1 for the topics that I leave out. I know that many of those topics *do* have some relevance to biology, but I judged that they had less relevance than what remained. Since most students (the non-majors) will see no more organic chemistry than what is in this course, it must be thorough enough for them to perform well on GRE, MCAT, and other standardized tests.

What does this leave? Everything else. Leaf through any standard organic text: the omissions in List 1 are actually only a small portion of what is covered in the text. There is still plenty left to study, and I assure you, students do not perceive what is left as an easy course!

Incorporating Biochemistry

Dropping the topics in List 1 leaves considerable time to cover biological applications. Since this is what the students came to hear, it makes no sense to wait until the very end to make these connections. (Of course, many connections *have* to wait until students have the background to understand them, but any applications that can be introduced early should be.) A brief list of topics that can be incorporated into this course, together with when they can be covered, appears in List 2. Others may choose to do things in a different order, or to add or subtract topics from this list.

Many of these topics are touched on in most organic courses, but the difference here is that these are integral parts of the course, not just throwaway topics. To students nothing is an integral part of the course unless it shows up on the exams.

List 1. Topics Left out of Bioorganic Course

- Free Radical Halogenation (NBS)
- Free Radical Additions
- Borane Additions
- Peroxide Workup of Ozonolysis
- Competition Between Strong and Weak o,p Directors
- Diazonium Salts
- Nucleophilic Aromatic Substitution
- Silyl Protecting Groups
- Industrial Polymers
- Diels–Alder Reaction
- Least Hindered Approach of Reagents
- Wittig Reaction and Other Ylids
- Wolf–Kishner, Clemmenson
- Organolithium Chemistry
- Organocopper Chemistry
- Diazomethane
- Acid-catalyzed Aldols
- Baeyer–Villiger Reaction
- Permanganate Oxidations
- Osmium Tetroxide Oxidations
- Periodate Oxidations
- Gabriel Synthesis
- Nitrile Chemistry
- Carbenes; Pericyclic Reactions

List 2. Biochemistry Topics Incorporated into Course

Hydrophilic and hydrophobic interactions; Protein Structure, DNA Structure, Lipid bilayers. This can be done during the introductory material, after discussion of intermolecular forces and hydrogen bonds.

Charges at Physiological pH. Also during the introductory material, in the section on acids and bases.

Cholesterol Biosynthesis from Squalene. Alkene addition reactions.

Chemistry of Vision. Spectroscopy provides an entry into what makes substances colored.

Intrinsic Asymmetry of Nature. Chirality section.

Disulfide Bonds in Protein Structure; Phosphates as Nature's Leaving Groups; Benzpyrene Epoxide. Alcohols and ethers.

NAD^+/NADH as Biological Redox Agent; Carbohydrates. The section on aldehydes and ketones lends itself naturally to these topics.

Glycolysis/TCA Cycle. We devote a separate section to the strategy of metabolic reactions. It serves as a great review of lots of functional group chemistry.

Amino Acids; Peptide Synthesis on Ribosome; Protein Structure: 1°, 2°, 3°. Section on nitrogen chemistry. Note some of this was introduced earlier and is reviewed here.

Hemes; DNA Structure. Section on aromatic chemistry.

Follow-up Organic Course

One of the beauties of this reshuffling is that all chemistry majors get a second shot at organic chemistry. Almost every school offers at least one advanced organic course of some type, but it is rarely required: only those students who are especially interested in organic chemistry take anything past sophomore organic. But a curriculum that starts organic with a bioorganic course can require all chemistry majors to fill in the holes left by that course, so everyone gets to review organic chemistry and then take it to the next level.

Are There Books for These Courses?

Not really. Although all the necessary topics are present in any standard sophomore organic text and any standard biochemistry text, the biochemistry text assumes students have completed the organic course, and the organic text does not leave topics out and saves the biochemistry for the end. To me, deleting topics from a book is problematic—the more you delete, the more often the text will discuss topics (and pose problems) that assume that the reader knows something that was discussed earlier. If something was skipped, the discussion (or problem) makes no sense to the student. I prefer to add to a book rather than subtract from it. The one-semester organic texts cover organic at too shallow a level, often leaving out mechanism and/or energy discussions in sufficient depth to be the basis of further study, hardly covering synthesis or spectroscopy with any rigor at all. Even the author's own text, which covers the appropriate topics in the appropriate order, does so at too low a level, since it was written for freshmen *(3, 6)*. However, it is likely that by speeding through the coverage of the general chemistry material presented in the first 6–8 chapters and expanding coverage of the biochemistry material presented later, it could serve the purpose. For the junior follow-up organic course, I would recommend using one of the normal sophomore organic texts, covering the material in one semester (since much of it is review).

Does It Work?

I cannot answer this question because I know of no department that has tried it. Juniata's curriculum does contain some of these aspects, but we teach the bioorganic course described above to first-semester freshmen. Indeed, some of this article has been adapted from my previous commentary describing that curriculum *(3)*. I continue to believe that teaching bioorganic to freshmen makes the most sense; however, a change of that magnitude requires an entire department to buy into the concept and to change what they have become comfortable doing. Reaching consensus on doing so is a monumental task, especially at large institutions. The change proposed here requires only the organic chemists and the biochemists to agree, and both can see obvious advantages: the biochemists get to talk about their field sooner and to a much larger audience, while the organic chemists get to talk about the nitty gritty to a much smaller audience—one that has been preselected to pay attention. I should point out that this ordering of material should do at least as good a job as the old organic course in converting biologists into chemists (one of the traditional roles of an organic course), since the organic chemistry presented is just as logical and challenging as it used to be but presented in a context that the biology students are predisposed to appreciate.

Is the Bioorganic Course Adequate Preparation for the MCATs?

I believe so. After taking this course in their first year, Juniata students get into medical school at a 95–100% rate. Since our course contains about six weeks of introductory (general) chemistry, they get less bioorganic than students will with this approach. It is true that most of our premedical students take a MCAT preparation course, where they may be exposed to a few reactions that were skipped in our course, but a thorough mechanistic understanding of what we cover allows them to pick up new material quickly; I believe that most premeds take such review courses. Further, the current MCATs rely much less on rote regurgitation of facts and more on interpretation of data, so lack of knowledge of certain topics should not harm the students. Our graduates continue to be as successful as ever in getting into and doing well in graduate and medical schools. The medical schools have made no objection to our curriculum. I believe that if anything, they should be pleased with this proposed switch.

Will CPT Buy This?

The CPT requirement is for the equivalent of three credits in biochemistry *(5)*. These credits do not have to be a separate course—indeed, the CPT encourages creative incorporation of biochemistry material into the core. The Juniata curriculum, as we teach it to freshmen, does not accomplish this because we have to teach six weeks of general chemistry at the beginning of the course before we can really get started. Accordingly, we have created a two-credit biochemistry course to complete the process. By compressing the general chemistry into one week, which should be easy in a sophomore course, one could expand the biochemistry content of the two-semester course to be at least two credits' worth. If several of the lab experiments that accompanied the course were biochemical in nature, I believe the CPT would accept this as sufficient.

Conclusion

I have described a reordering of the organic/biochemistry material that should be applicable at almost any institution. The revised courses should be more useful and relevant to the majority of our audience while maintaining and possibly improving the education of chemistry majors.

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textbook *(6)*. The Howard Hughes Medical Institute also contributed to the curriculum development process.

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