In Focus
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# Bringing the Excitement of Biological Research into the Chemistry Classroom at MIT

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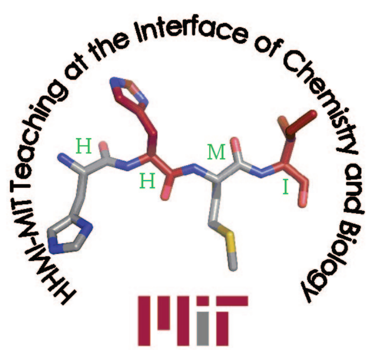
All Massachusetts Institute of Technology (MIT) undergraduates are required to take introductory chemistry, which means that their willing or unwilling ears are ours for a full semester. MIT therefore has the unique opportunity to instill an appreciation of chemical principles in every incoming student, including those who left high school with an ambivalent or negative view of chemistry. Two classes within the chemistry department fulfill MIT's basic chemistry requirement, with the more advanced course attracting the majority of those students already excited about chemistry. Here, we discuss our plans for the *other* course, Principles of Chemical Science 5.111, which is composed of students who are generally not planning on chemistry or engineering majors, ~25% of each freshman class. Among this group, there is considerable interest in biology. Many students express a passion for cancer research and the biology of disease but claim they "hate chemistry". Few understand that chemical reactions are at the heart of biological processes, from the workings of a cell to the inhibition of cancer targets. By demonstrating the relationship between chemistry and biology, we hope to harness the students' enthusiasm for biology and medicine to increase their interest in and understanding of chemistry.

This enriched introductory chemistry course is central to a larger initiative, funded by the Howard Hughes Medical Institute (HHMI) Professors Program, aimed at increasing the understanding of chemical principles among biology students and demonstrating the vital connection between biology and chemistry. Similar to the overall program goals, our hope for the course is to foster an understanding of chemistry's relevance by illuminating the centrality of chemistry in biological and medicinal research. Although scattered biological examples have been part of our curriculum for several years, this fall will mark the first full run of the more biologically focused course. In this article, we outline the changes that have been implemented and the feedback we have thus far received. With an assessment plan in place, we look forward to reporting successes and pitfalls as the program continues.




**Course Material.** In compiling biologically enriched material for the freshman chemistry course, our intent is not to create a combined chemistry and biology course or even to change the current curriculum, which has been set by the MIT chemistry department. Instead, our approach is to invigorate the lectures and associated problem sets with biological examples that illustrate each concept presented. We hope that the placement of relevant examples and research applications of a given chemical principle will give new context to the course material. This approach has already been implemented on a smaller scale by presenting several biological examples per semester that bring the excitement of research into the classroom. For example, in teaching about the 3D

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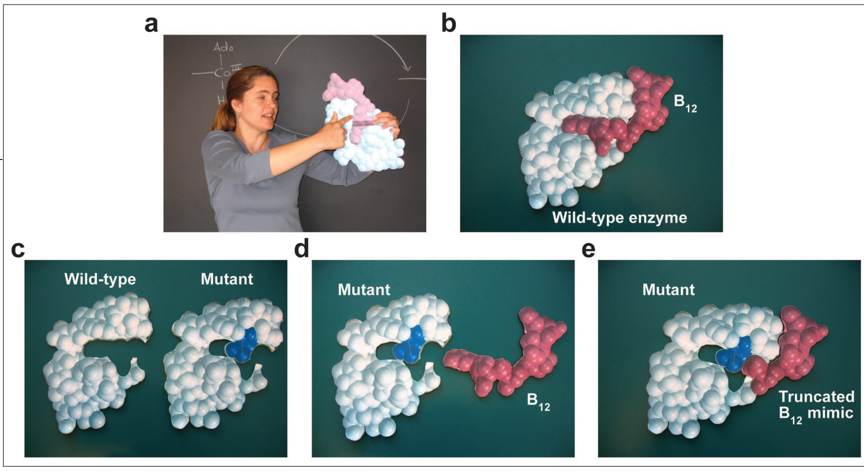


**Figure 1. Molecular shape illustration. a) Cardboard cutouts are used for an in-class demonstration. b) Vitamin $B_{12}$ (red) fits into the binding pocket of the wild-type methylmalonyl-CoA mutase (light gray) to make an active complex. c) The problematic arginine residue (dark blue) in the mutant enzyme blocks the $B_{12}$ binding pocket. d) $B_{12}$ (red) cannot bind to the mutant enzyme. e) A smaller $B_{12}$ mimic (red) may be able to bind to the mutant enzyme to form an active or partially active complex. Images courtesy of Elizabeth Vogel Taylor.**

shapes of molecules, we present some structural research on the genetic disorder methylmalonic aciduria, which is a metabolic disease that can result in developmental retardation and infant mortality (*1*). A single amino acid mutation in the metabolic enzyme methylmalonyl-coenzyme A (CoA) mutase leads to this condition, and the class example encourages students to consider how comparing the shapes of the different amino acid side chains can explain the mutant enzyme inactivity and inspire an innovative treatment strategy (see Box 1 and Figure 1). Even on this small scale, the application of chemical principles to biology was met with enthusiasm by the students. Many commented in the course evaluations on the value of "connecting different subject areas" and providing an "application of the topics to the real world". Students not only "definitely liked [the] life science (*e.g.*, biochem) examples" but also requested additional examples on more varied topics throughout all of the units. Several students expressed the encouraging sentiment that, prior to this course, chemistry was their least favorite of all the sciences, but now they're interested in taking more chemistry courses.

Because incorporating the biological examples requires minimal additional class time, the students can gain context and motivation without losing out on any of the chemistry details already in the curriculum. Starting this year, the problem sets will also include biological connections. The assignments will not be lengthened, but they will incorporate biology and research-like inquiries into pre-existing problem types. By presenting the new material as part of graded problem sets, we hope to convey to the students that biological applications of chemistry are not "supplementary" or "optional" materials and that by understanding chemistry it is possible to approach and understand questions in biology. The course teaching assistants (TAs) will be involved in developing some of the biochemistry- and chemical-biology-based problems for the problem sets, and we hope to generate a diverse set of problems based on the individual interests and expertise of the contributors.

**TA Training.** The Principles of Chemical Sciences course at MIT has ~250 students every fall semester. The full class meets for lecture three times a week, and the class breaks into groups of ~20 students for twice-weekly recitation sessions run by graduate student TAs. Typically, the TAs for the course are first-semester chemistry graduate students. Recognizing that TAs have a huge impact on the experience of students in large introductory courses and that these new graduate students are the chemistry teachers of the future, we have introduced an expanded TA training program for the course. The TAs will participate in a week-long "boot camp" in late August that covers topics such as interdisciplinary teaching, team building, and basic biochemistry and chemical biology, with a special focus on teaching some of the more difficult concepts for the students, including acid–base problems. We will use *Scientific Teaching*, a book written as part of Jo Handelman's HHMI professorship, to cover active learning techniques and diversity issues (*2*). This boot camp will supplement a shorter TA training that is offered to all incoming graduate students and should help develop a cohesive group of TAs for the course. We hope to demonstrate that by investing some extra time for TA training at the start of the semester, it is possible to develop a group of TAs that will better teach the material, be enthusiastic about the biological applications, and have a network of other TAs for support and guidance.

To recruit a dedicated group of teachers, we advertised the course as a new teaching opportunity during accepted-students weekend and invited applications from incoming graduate students. We did not require that the TA applicants have any prior biology background but instead sought out highly motivated and enthusiastic teachers. In past years, freshman chemistry has been viewed as an undesirable teaching assignment, because more specialized classes are regarded as better preparation for qualifying exams and graduate course work. However, this year 25% of the incoming graduate students applied for a TA position for the biologically enriched introductory chemistry course, a sharp contrast with previous years' experiences. We attribute this change in attitude to the focus on teacher training, the increasing interest among graduate students in the interface between biology and chemistry, and the opportunity for the students to be part of a prestigious HHMI initiative. An unanticipated benefit of these TA positions may be in recruiting prospective graduate students to MIT who are passionate about teaching. In her application, one of this year's TA candidates stated that "knowledge of the HHMI TA program was an important factor in my decision to come to MIT."

**An Updated Understanding of Chemists.** Along with conveying the inextricable relationship between biology and chemistry and reflecting the way scientists think about research, this course will present to students a concrete vision of who chemists are, including women and individuals of all ethnic and socioeconomic backgrounds. Although the material will not be completed for this fall, we plan to create and incorporate short video clips of "real scientists" into the PowerPoint lectures. We hope to eventually compile a number of very brief videos (1–2 min each) that show graduate students in all disciplines discussing the importance of a chemical concept from the course in their graduate research. Because undergraduate students are often unaware of what career opportunities are open to those with a chemistry degree, we are also planning to present short clips of former chemistry majors discussing their chosen careers.

**Beyond Freshman Chemistry.** As part of our HHMI educational grant, several other initiatives have begun at MIT to encourage and support students interested in both chemistry and biology. Because MIT does not offer a biochemistry or chemical biology major, the MIT Undergraduate Biochemistry Association (MUBA) was created as an academic and social resource for students interested in any aspect of those disciplines. MUBA offers academic advising on interdepartmental course selection and research opportunities, and MUBA members organize a number of events every year, including faculty dinners, community outreach, biotech tours, and seminars on career and graduate school opportunities. Currently, >80 MIT undergraduates are involved in MUBA with majors that include chemistry, biology, brain and cognitive science, chemical engineering, biological engineering, and physics.

In addition, we are now midway through our first year of an HHMI–MIT summer research program in chemical biology, which places undergraduate students from both MIT and colleges around the country in MIT laboratories. The students work for 10 weeks during the summer in research groups that self-identify their work as at the interface of chemistry and biology. This year's program includes eight undergraduates who conduct research and attend biweekly seminars and 10 graduate student or postdoctoral mentors who concurrently participate in a six-session mentoring seminar. MUBA and the chemical biology summer research program provide MIT students additional opportunities to pursue their interests in biochemistry and chemical biology once they have completed the introductory chemistry course.

Ideally, these initiatives will help to generate an appreciation of chemistry among other life scientists and nonscientists, encourage an appreciation of biology among chemists, and inspire some students to pursue research at the interface of chemistry and biology. As research becomes increasingly interdisciplinary, an understanding of related fields will be essential for productive research collaborations.

**Box 1. An Application for Understanding Molecular Shapes**

Methylmalonyl-CoA mutase is a vitamin $B_{12}$-dependent enzyme that catalyzes an essential step in the breakdown of fatty acids to energy. Inherited defects in the methylmalonyl-CoA mutase gene can lead to production of an inactive enzyme, resulting in organ failure, retardation, and even death from buildup of metabolic intermediates and other toxic materials in the body. Some mutants regain activity after addition of high concentrations of $B_{12}$, an indication that the mutations cause low (but not completely destroyed) $B_{12}$ affinity. However, one particular mutant with an arginine amino acid in the place of a glycine lacks all enzymatic activity and cannot be activated with high concentrations of $B_{12}$. Using crystallography to visualize the mutant and wild-type structures of the enzyme, scientists were able to determine that the glycine to arginine mutation occurs within the $B_{12}$ binding pocket and that the size and position of the arginine is sufficient to block binding of $B_{12}$, which is essential for making a functional enzyme complex. The development of a $B_{12}$ mimic that excludes the moiety that "fits" in the mutant's blocked pocket could lead to a cure by partially restoring the activity of the enzyme–$B_{12}$ complex.


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