Evolution across the Curriculum: Microbiology

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An integrated understanding of microbiology and evolutionary biology is essential for students pursuing careers in microbiology and healthcare fields. In this Perspective, we discuss the usefulness of evolutionary concepts and an overall evolutionary framework for students enrolled in microbiology courses. Further, we propose a set of learning goals for students studying microbial evolution concepts. We then describe some barriers to microbial evolution teaching and learning and encourage the continued incorporation of evidence-based teaching practices into microbiology courses at all levels. Next, we review the current status of microbial evolution assessment tools and describe some education resources available for teaching microbial evolution. Successful microbial evolution education will require that evolution be taught across the undergraduate biology curriculum, with a continued focus on applications and applied careers, while aligning with national biology education reform initiatives.

“Evolution of large asexual cell populations underlies 30% of deaths worldwide, including those caused by bacteria, fungi, parasites, and cancer.”—Levy et al., 2015 (27)

INTRODUCTION

From antibiotic resistance to vaccine production, evolution underlies modern microbiology. Thus, a working knowledge of microbial evolution is essential for careers in biology and healthcare. Microbial evolution drives antibiotic resistance (12, 27), and evolutionary principles are used for vaccine production (13, 27), synthetic biology, evolutionary engineering (12, 27, 43), and industrial fermentation (8, 15). In addition, because microbial evolution follows the same principles of evolution as other large asexual populations, its understanding may also be applied to the within-individual evolution of cancer (16, 23) and the emergence of new human viruses (45).

The rise of these modern challenges requires student preparation in both the biomolecular sciences and evolutionary biology. Perhaps more critical, however, is the need for students to be able to synthesize their knowledge in these areas. Students must be able to interpret and analyze data on evolving systems (such as evolution and cancer) to understand the complexity of these problems and make predictions about what evolution will do in the future.

In this Perspective, we argue that evolution is often missing from the study and teaching of microbiology. Further, we discuss barriers to microbial evolution instruction and offer suggestions for incorporating evolution in undergraduate microbiology curricula. Our goal is to provide a framework in which microbiology instructors can integrate evolutionary biology practices into their courses while preparing students for contemporary careers in the biological sciences and healthcare.

DISCUSSION

Evolution is often missing from microbiology discourse and education

Despite its importance to human health and industry, evolutionary thinking and language surprisingly are often missing from academic and non-academic discourse on these topics (2). Authors of the primary literature often omit evolution, even in cases where the role of evolution is obvious, such as antibiotic resistance (2). Evolution is also
missing from official descriptions of antibiotic resistance from reputable agencies such as the Centers for Disease Control (CDC) and the Food and Drug Administration (FDA), reinforcing the incorrect idea that evolutionary biology is not relevant to microbiology. For example, the FDA’s description of antibiotic resistance contains no mentions of the word “evolution” or any of its derivatives (FDA [http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/ucm134455.htm]). The CDC’s “Antibiotic Resistance Threats” report similarly omits evolution in an incorrect description of how resistance happens: “Simply using antibiotics creates resistance” (CDC [www.cdc.gov/drugresistance/threat-report-2013/]). Articles in the popular press also omit evolution in cases where it should be highlighted, such as Frontline’s 2013 “Hunting the Nightmare Bacteria” (Frontline Program [www.pbs.org/wgbh/pages/frontline/hunting-the-nightmare-bacteria/]), which describes simply the vague “spread” of resistance with no mention of evolution.

One reason why an evolutionary perspective may be missing from public discourse is that biology education tends to be compartmentalized. Evolution is often sequestered in specific courses or class periods rather than being integrated throughout the curriculum. This pattern is consistent with the isolation of evolution concepts in dedicated textbook chapters (33) and continues as students specialize in different majors. Students of general biology, ecology, and evolution often take an additional, evolution-specific course rooted in natural history (with little mention of microbes), while biomolecular students go on to take microbiology-specific courses, often with little mention of evolution.

**Barriers to effective teaching and learning of microbial evolution**

Microbial evolution education presents specific challenges involving unique barriers to learning. These include: confusing terminology, patterns of language use among biology experts, misinformation from the media, and perceptions of controversy. In this section, we first define key terms that vary in their definition and usage across biology and suggest ways to avoid language confusion between subdisciplines. We then discuss some deeper philosophical reasons why biological language often undermines evolutionary thinking. Finally, we provide examples of incorrect evolutionary reasoning and discuss how perceptions of conflict impede instruction.

In some cases, language use is confusing because words have multiple meanings within biology or between biology and common usage (28, 29, 39). Table 1 provides a list of key definitions as used by evolutionary biologists, as well as examples of misuse and alternative definitions—in particular within microbiology—and suggestions for avoiding confusion when combining evolutionary biology and microbiology. For example, the term “drift” has two radically different—even opposite meanings—in evolutionary biology and influenza biology. Evolutionary biologists use the term drift, short for genetic drift, to refer exclusively to random changes in population composition, distinguishing it in a fundamental way from those changes favored by natural selection (48). But in the influenza literature (for representative examples, see refs 6, 9, 21, www.cdc.gov/flu/about/viruses/change.htm) the word drift is used to indicate changes to the flu virus accumulated over time, including both changes favored by natural selection and changes due to the random evolutionary process of drift. To nonexperts, including undergraduate students, the way to avoid confusion about these terms is to be explicit when talking about processes, referring to “genetic drift” when discussing evolutionary processes and giving a reminder about its random nature, and then being open and clear that the term has two different, confusing meanings when discussing influenza’s “drift.” In addition to drift, we have encountered many other potential sources of confusion in biological language. These are listed and described in Table 1 and include such seemingly straightforward terms as variation, selection, evolution, adaptation, and homology.

Teleological language is language that evokes purpose, design, intent, or future outcome to explain phenomena (42) and is common throughout biology, for example when biologists refer to an organism doing something because it “needs to.” Evolutionary biologists often use phrasing that involves teleological language taken metaphorically or used as shorthand for natural selection (Allen, Colin, “Teleological Notions in Biology,” The Stanford Encyclopedia of Philosophy (Winter 2009 Edition), Edward N. Zalta (ed.) [http://plato.stanford.edu/archives/win2009/entries/teleology-biology/]). As biologists, we need to remind ourselves to speak about evolution in ways that are clear to nonexpert students, including replacing our teleological language with naturalistic language. Using non-teleological language will help prevent reinforcement of the misconceptions that organisms adapt because they “need to” and that mutations happen due to selection. Using non-teleological phrasing also requires specifying evolutionary mechanisms, reinforcing a conceptual model of natural selection (see Table 1, “Selection”). For example, one may replace the teleological statement, “The organism needed to evolve resistance,” with the naturalistic statement, “Selection favored the growth of resistant organisms over sensitive organisms.”

In some cases, evolution is simply missing from discourse, as if the word itself were taboo (2). In other cases, incorrect or incorrectly qualified information hinders learning. Surprisingly, misinformation frequently appears from regarded authorities on biological concepts. For example, in the introduction, we used the CDC’s antibiotic resistance threat report (www.cdc.gov/drugresistance/threat-report-2013/) example on antibiotic resistance to point out the absence of evolutionary thinking. While the description overtly omits evolution, it also incorrectly states, “Simply using antibiotics creates resistance.” The statement implies mutations are due to the use of antibiotics, suggests that evolution is intentional, and largely ignores the complexity of evolutionary and ecological factors in the antibiotic resistance problem.
**TABLE 1.**
Terminology in evolutionary biology.

| Term; Evolutionary Biology Definition | Misleading, Confusing, or Incorrect Definitions and Examples of Misuse | Suggested Changes or Clarifying Language for Common Usage |
|---------------------------------------|---------------------------------------------------------------------|--------------------------------------------------------|
| **Evolution:** The process by which populations change over time. | The process by which *individuals* change over time. 1) Iconic image of ape → human 'evolution.' 2) "She evolved during grad school" (indicating learning, personal growth, change, etc.) | Talk only about evolution happening to populations. Point out it does not happen to individuals. Use "learning," "growth," "change," etc., when talking about individuals. |
| **Microbial Evolution:** The process by which microbial populations change over time. | Sometimes incorrectly used interchangeably with "microevolution." | Don’t call microbial evolution microevolution, or vice versa. |
| **Microevolution:** Bucket term with several definitions: 1) "small" evolutionary changes, such as those caused by beneficial point mutations—note this definition is identical to simply using "evolution"; 2) allele frequency changes—note this definition is also identical to simply using "evolution"; 3) that which is not macroevolution (speciation, often applied when talking about phylogenies). | "Microevolution" is sometimes used in a way that seems to belittle the evolutionary processes observed in empirical biology. E.g., "Evolution experiments only result in microevolution." | Avoid use of "microevolution" where simply using "evolution" will do, which is most of the time. Whether changes are small or large, evolution is evolution. |
| **Emergence:** A general term that loosely means the appearance of previously uncharacterized pathogens. The term lacks specific utility because it lumps together both ecological and evolutionary factors in epidemiology. | "Emergence" is often used as a vague alternative to more specific terms, such as "evolution." See (2) for a useful critique of this usage. | Use "evolution" where possible. Use "emergence" only when the ecological and evolutionary factors in disease epidemiology are unclear, and clarify that point for students and nonexperts. |
| **Randomness:** A property of any stochastic process. Evolutionary biologists often use the term to describe how mutation occurs without the influence of selection. | Commonly used arguments of the type: "Evolution is just random, but the natural world is complex, therefore evolution cannot be true." Some (especially younger) people now commonly use this to mean "unexpected" or "weird." | Pair thinking about random genetic variation with thinking about selection, which is not random. Logically, the result is a process that must not be random. Clarify that mutation is random, but evolution by natural selection is not. |
| **Variation:** Differences among organisms within a population. Mutations and horizontal gene transfer produce heritable genetic variation. Evolutionary biologists most often discuss heritable genetic variation but some measure how all variation (heritable or not) changes due to selection (25). | Variation in the environment. | Use "variation" to refer to differences among organisms within a population. Use "different" or "unique" to differentiate among separate environments. Use "fluctuating" or "stochastic" to describe environments that change through time. |
| **Inheritance:** The process by which genetic information is passed from parent to offspring. Specifically, inheritance is considered "particulate" (encoded by discrete genes, as discovered by Mendel). | Darwin himself incorrectly conceptualized inheritance as "blended" (offspring would simply have characteristics that are a blend of their parents), which would tend to reduce variation on which selection may act (10). | Discuss the discrete nature of inheritance in a history-of-science context (e.g., Darwin’s vs. Mendel’s models) and why this idea is important to the study of evolution. |
Another example from the Introduction was the FDA’s explanation of antibiotic resistance, which not only contains no mention of the word evolution, but also confusingly groups together both heritable and non-heritable sources of antibiotic resistance (FDA [http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/ucm134455.htm]). The FDA’s list includes de novo mutation, transduction, conjugation, and efflux; the first three processes have the potential to change the genome, and thus are heritable. Although de novo mutation or horizontal gene transfer may result in a bacterium capable of the fourth process (efflux), antibiotic efflux itself is simply a phenotypic response to antibiotics, and not a heritable source of variation on which selection may act.

A wealth of misinformation is also available from pseudoscience movements involving creationism and intelligent design. However, this topic is beyond the scope of this Perspective and has been covered extensively elsewhere; we...
discussed in the Introduction, including antibiotic resistance, in Table 2. These learning goals cover some of the topics applications and a molecular evolution synthesis is shown microbiology learning objectives involving contemporary, a broader survey of microbial evolution topics. A set of premedical students might include topics in evolutionary, for example, specific areas covered in courses taken by may be more or less specific depending on the classroom. The Robson-Burns questions use examples from microbes and macroscopic organisms, as the underlying concept of mutation timing is the same regardless of species. Similarly, tools that were constructed to assess natural selection without specific consideration of microbes are also somewhat useful for microbial evolution. These include the Concept Inventory of Natural Selection (CINS; 1) and the Assessing Contextual Reasoning about Natural Selection tool (ACORNS; 32). In contrast to evolution-focused tools, the Genetics Concept Assessment (GCA; 45) and the Molecular Life Sciences Concept Inventory (MLSCI; 22) assess topics covered in undergraduate genetics and biochemistry courses, respectively. Although both the GCA and MLSCI include items relevant to genetics of asexual populations, including microbes and cancer, the assessments have been validated as whole units for their specific purposes, so the validity of using subsets of questions is unclear.

An ideal assessment tool for microbial evolution would cover basic research and applications-based learning objectives relevant to modern students’ future careers (Table 2). Assessment items would be constructed in a way that avoids potential ambiguity of terminology interpretation, as in common misuses of terms shown in Table 1. Some of the items would likely cover topics similar to those appearing in other assessments. For example the Robson and Burns assessment (41) extensively covers mutation timing, while the Genetics Concept Assessment (45) contains an item about the heritability of cancer mutations. Concept inventories typically assess respondents’ knowledge of a specific content area and comprise multiple-choice questions with both correct and common distracter answers. Therefore, a microbial evolution concept inventory might be especially useful to assess students’ correct ideas as well as misconceptions. However, conceptual strength and depth of student learning would be assessed more thoroughly with qualitative assessments involving open-ended responses, construction of visual models, and oral interviews.
Teaching materials for microbial evolution education vary by suitability for different classroom levels, student experience, and instructor preparation. For example, some activities require microbiological laboratory equipment, student exposure to microbial genetics, and instructor readiness for inquiry-based classrooms. Many of the resources may be used for scaffolding higher-level learning objectives (Table 2).

In a talk on evolution across the curriculum, Gordon Uno advised: “Evolution—say it everyday” (36). When we begin thinking and speaking evolutionarily, our language and teaching of evolution will become clearer for our students as well. Thinking evolutionarily is the first step in this direction for instructors of any biology course at any level, from introductory biology to special topics in molecular biology.

In a nonmajors course on emerging infectious diseases, Fass aligned classroom activities to core themes of ASM’s microbiology curriculum recommendations (the precursor to ASM’s 2012 guidelines: www.asm.org/index.php/guidelines/curriculum-guidelines), with evolutionary concepts.

| Microbiology Application | Learning Objective | Activities and Resources |
|--------------------------|--------------------|-------------------------|
| Antibiotic resistance    | Given a description of an antibiotic-sensitive bacterial pathogen, students will be able to describe and predict the evolution of antibiotic resistance, including specific roles of de novo mutation, horizontal and vertical gene transfer, and antibiotic presence in the environment. | Evolutionary processes and language of antibiotic resistance review (2) | Antibiotic resistance case study for the classroom (11) |
|                          |                    |                         | Teaching emerging diseases (14) |
|                          |                    |                         | Antibiotic resistance classroom evolution experiment (24) |
|                          |                    |                         | Teaching random mutations and antibiotic resistance (41) |
| Industrial fermentation   | Using information about an industrially important microbe and its fermentation products, students will be able to plan an experiment to evolutionarily engineer increased production of a specific fermentation product, involving serial passaging, an appropriate selective environment, and potential sources of conflicting selection. | Classroom evolution experiment with bacteria (24) | Bacterial fitness classroom exercise (35) |
|                          |                    |                         | Yeast evolution classroom activity (38) |
|                          |                    |                         | Evolutionary engineering microbes review (43) |
|                          |                    |                         | Yeast mutation timing (44) |
| Human viruses            | Students will be able to use information about a newly characterized pathogenic virus and its host environment (host species and density, mode of transmission, climate, and interactions with other species and the environment) to make predictions about the virus’s future evolution, including immune escape, evolution of increased or decreased virulence, and drug resistance, and explain the selection pressures and potential mutations leading to these phenotypes. | Teaching emerging diseases (14) | Influenza evolution review (46) |
| Cancer                   | Given data about the mode of action of anticancer drugs, students will be able to predict similarities and differences among cases of cancer evolution within patients, including drug resistance and virulence genotypes and phenotypes. When prompted on heritability of those mutations, students will accurately indicate which cell lines and progeny will inherit the cancer-associated mutations. | Linking mutations and cancer (19) | Cancer evolution review (23) |
| Vaccine production       | Students will be able to interpret a traditional model of viral attenuation and vaccine production to describe why the virus is non-pathogenic, specifically including the roles of de novo mutation, generations, selection, and evolutionary trade-offs. | Parasite evolution review (13) | Virus mutation classroom activities (17, 41) |

References include resources useful for scaffolding learning for each objective, discussed in the main text.
addressed throughout the course (14). The article is a case study in curricular reform incorporating microbial evolution and emerging diseases, using a mix of reference materials for student reading. Cloud-Hansen et al.'s case-based unit “Citrate Use case (20) is one of six free online modules students can work through either on their own or as part of a classroom exercise (www.evo-ed.org/). Each of the six unique cases is based on real research and describes the evolutionary processes involved from mutations at the DNA level to the fixation of alternate adaptive phenotypes. The E. coli Citrate Use case is appropriate for introductory biology students or upper-level students and works particularly well as part of more detailed lessons on gene regulation and molecular evolution.

Several instructors have used laboratory classroom exercises to demonstrate basic evolutionary processes. Based on their own research, Ratcliff et al. provide free kits and methods for laboratory experiments involving the evolution of multicellular yeast (38). The exercise can be adapted for high school and undergraduate classrooms equipped with laboratory space. Handelsman et al.'s undergraduate classroom exercise “Are chemicals, mutations, and cancer linked?” (19) employs inquiry-based learning with a modified Ames test to prompt student exploration of chemical mutagenicity. For classrooms without microbiological laboratory set-up, Lark et al. present an Avida-ED (http://avida-ed.msu.edu/) activity to investigate the effects of mutation rates on mutant frequencies (26).

A topic of central interest to both evolutionary biology and microbiology is mutation timing, and many instructors have brought the classic Luria-Delbrück fluctuation test into their classrooms. Robson and Burns (41) studied how the Luria-Delbrück experiment increased students' conceptions of mutation timing and demonstrated student learning with a formal assessment. Green and Bozzone (17) and the University of Washington Biology 481 course website (http://kerrlab.org/Bio481/HomePage) offer additional detailed lesson plans to teach mutation timing with microbes, and Smith et al. more recently have done so with yeast (44). Mutation timing experiments with microbes are appropriate for upper-level inquiry-based courses equipped with microbiology labs. For non-equipped classrooms, the lesson may be taught in an inquiry-focused manner using the digital evolution computer program Avida-ED (http://avida-ed.msu.edu/).

While knowledge of mutation timing provides a foundation for conceptualizing natural selection, evolution experiments provide direct demonstration of it. Experimental evolution methods are especially relevant to antibiotic resistance and industrial engineering. These exercises all require microbiological laboratory classroom set-up and are generally best suited for upper-level courses, although some instructors are beginning to use similar methods in introductory biology courses (B. Kerr, personal communication). In addition to published protocols on GASP mutant and antibiotic resistance evolution experiments for undergraduate laboratory courses (24, 35), non-published evolution experiments for the undergraduate classroom can be found at MicrobialEvolution.org, a repository for unpublished microbial evolution education resources. The site is the collaborative effort of microbial evolutionary biologists and invites all instructors to upload and share unpublished resources and course materials.

CONCLUSION

Understanding microbial evolution requires the integration of evolutionary biology and molecular biology principles. Synthesizing these two subdisciplines promises to prepare students to solve contemporary problems in microbiology, including how to control the spread of antibiotic resistant bacteria, how to predict human pathogen emergence, the evolution of metastasis in cancer patients, and the complex dynamics of industrial fermentation processes (Table 2). These problems are real and serve to motivate learning of microbial evolution, appealing broadly to students moving into healthcare professions, basic research, and applied biology.

Our hope is that tools allowing the assessment of learning gains related to objectives specific to microbial evolution will be available in the near future. Curricular reform will require time and effort, and topical changes will need to be made along with other classroom changes to accommodate learning that is more inquiry-based yet still rigorous with respect to mastery of fundamental content knowledge. If these endeavors are successful, twenty years into a rosy future, our current students will be at the peaks of their careers, applying evolutionary thinking to complex problems and passing on their knowledge and skills to the next generation of biologists.

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