

## Epigenetics for the 21st-Century Biology Student

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**Epigenetics, a rapidly emerging biological science, investigates changes in gene expression without any change to the primary DNA sequence. Epigenetics plays an important role in diverse areas, including nutritional sciences, psychology, and environmental sciences. In addition, epigenetic phenomena are closely implicated in various diseases, including cancer and neurological disorders. Even though the importance of epigenetics has been widely discussed in the literature, there is no quantitative assessment on the development of epigenetics. In this paper, we show our metadata analysis of PubMed to quantitatively measure the temporal development of epigenetics. Our analysis indicates that the publication volume of epigenetics will reach 20.7% of all genetics paper in 10 years (year 2029). Based on our analysis, we suggest that epigenetics be added to the biology undergraduate curriculum.**

### INTRODUCTION

Optimization of curriculum is an essential task in any academic discipline. It is especially so for rapidly developing fields such as the biological sciences. We believe that the readers of the *Journal of Microbiology and Biology Education* are attentive to optimizing their curriculum so that it can meet the needs of present and future students. In this paper, we share our perspective on an emerging biological science, epigenetics, as a potential subject of undergraduate education. We think that it is important to highlight epigenetics, considering that it does not receive appropriate attention in the higher education institutions. For example, according to our search conducted in December 2018, while most of the 26 universities and colleges in the state of Georgia have courses on genetics, only three institutions offer epigenetics courses (data are available upon request). Of course, being absent in the course catalog does not necessarily mean that epigenetics is completely ignored, as it can be taught as a part of other courses. Furthermore, one may view epigenetics as a non-core subject in undergraduate biology education. According to the Educational Testing Service (ETS; <https://www.ets.org>), which administers the *Major Field Test* that measures students' knowledge in their undergraduate study in the United States, biology is divided into four major fields: cell biology; molecular biology and genetics; organismal biology;

and population biology, evolution and ecology ([https://www.ets.org/s/mft/pdf/mft\\_testdesc\\_biology\\_4kmf.pdf](https://www.ets.org/s/mft/pdf/mft_testdesc_biology_4kmf.pdf)). Following the view of the ETS, epigenetics may be treated as a specialized subject in biology. Therefore, it may be appropriate to compare course offering of epigenetics with other non-core biology subjects. When this paper was reviewed, reviewers compared epigenetics with immunology as an example of such non-core subjects. We examined the status of immunology for its offering in curriculum, and found that immunology is offered in many institutions, unlike epigenetics (data are available upon request).

### Brief introduction to epigenetics

Profiling of gene expression is one of the central subjects in modern biological research (1). Scientists have found that gene expression profiles can be reprogrammed at precise points during development or in response to environmental or psychological factors (2), resulting in a field of research called epigenetics. Epigenetics refers to changes in gene expression without any change to the primary DNA sequence (3). The Greek root *e*pi indicates gene expression over or above the genetic material. Genes can be turned “on” and “off” via various epigenetic mechanisms, such as DNA methylation and histone modifications, resulting in phenotypic changes (4–6). One of the most remarkable features of epigenetics is that its effects can be inherited by the next generation, unlike other mechanisms of gene regulation (7). Modern understanding of epigenetics continues to expand on all the initial discoveries, as interest in epigenetics has exploded in recent years (8). A few recent examples of the application of epigenetics can be found in the research pertaining to human diseases such as diabetes (9),

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cancer (10), and autism (11), where epigenetic mechanisms such as DNA methylation are suggested as being implicated in pathogenesis.

## PROCEDURE

In our previous papers (12–14), we showed that the importance of a certain biological science can be measured based on the number of peer-reviewed publications in that discipline. In those studies, several interdisciplinary biological sciences (biochemistry, biophysics, bioinformatics, and systems biology) were examined using the quantity of publications in those fields by searching the PubMed database (<https://www.ncbi.nlm.nih.gov/pubmed>) to assess the development of each subject (12, 13). In this study, we took the same approach to quantitatively describe the temporal progress of epigenetics. We, then, compared it with its closely related discipline, genetics, which is a well-established core subject in terms of research as well as academic curriculum. In the search, epigenetics or genetics articles were defined as those containing “epigenetics OR epigenetic” or “genetics OR genetic” in the title/abstract, respectively. The search gave us the number of articles being published and indexed in PubMed each year up to 2017 for the two fields (Fig. 1A and B). Each plot clearly shows that both genetics and epigenetics have been proliferating. In order to compare the growth of epigenetics with that of genetics, the number of publications in epigenetics was normalized to that of genetics for each year, beginning with 1963 (Fig. 1C). To describe the trend of epigenetics relative to genetics quantitatively, a nonlinear fitting was performed and a sigmoidal function (Eq. 1) was found to best fit to the data:

$$y = \frac{a}{1 + \exp[(x_0 - x)/b]} \quad (1)$$

where  $x$  is the year and  $y$  is the normalized number of epigenetics papers (%). The fitting parameters  $a$ ,  $b$ , and  $x_0$  are 21.5, 5.4, and 2011.5, respectively. The mathematical meaning of those parameters can be found in our previous paper (13). Interestingly, the same type of sigmoidal function (Eq. 1) was found to be effective in describing the development of biophysics, bioinformatics, and systems biology as well (13), suggesting that sigmoidal behavior may be a general feature in the development of biological disciplines. Based on the parameter values, we can predict the relative importance of epigenetics in the near future. If the trend of both epigenetics and genetics exhibited in the last 50 years is maintained in the future, the relative importance of epigenetics in five years (year 2024) will be 19.6%, which is a noticeable increase from 15.8% at year 2017. In ten years (year 2029), it is expected to be 20.7%. Considering the central importance of genetics in the biological sciences, the significance of epigenetics in the near future is evident. Therefore, to prepare students for the future, it is highly desirable to implement epigenetics into undergraduate curricula.

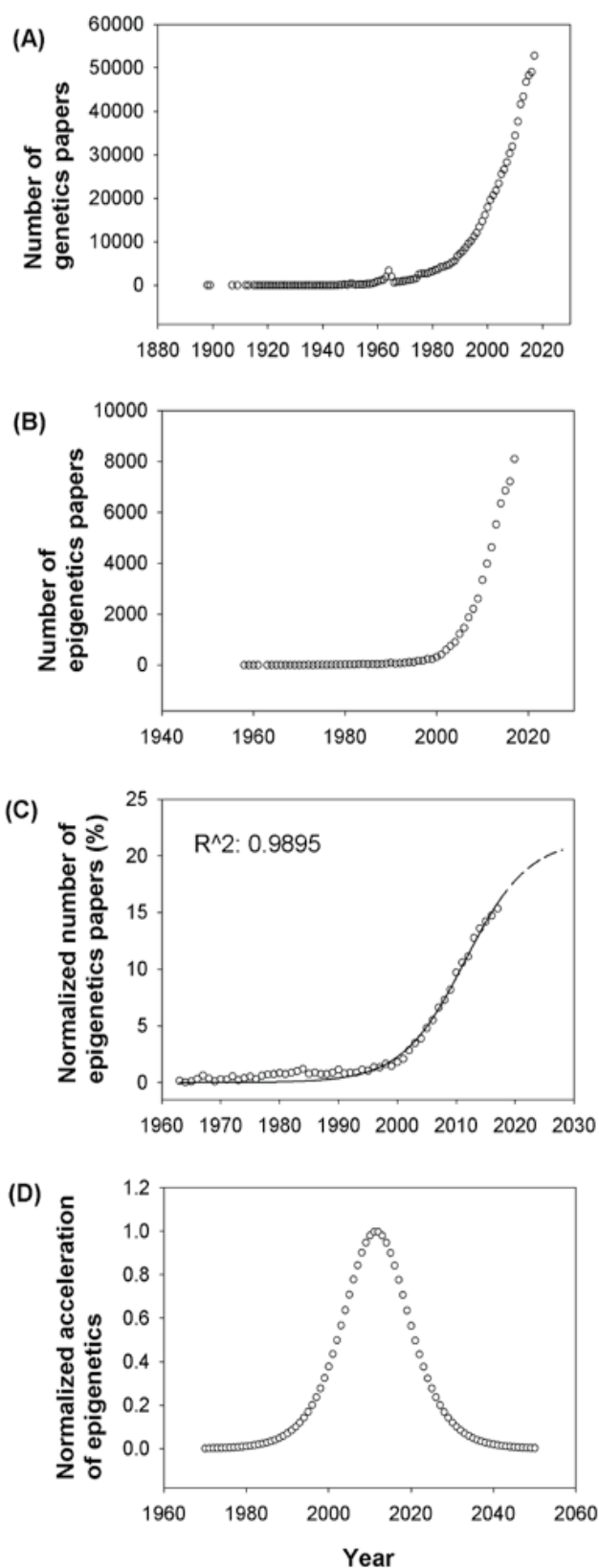


FIGURE 1. Publication trend in genetics (A) and epigenetics (B) and normalized publication data of epigenetics (C) in PubMed. Acceleration in the temporal progress of epigenetics is shown in (D).

Another utility of Eq. 1 is that its derivative with respect to  $x$  (Eq. 2) will characterize the underlying force of the development of epigenetics, helping visualize the long-term dynamics of epigenetics.

$$\frac{dy}{dx} = \frac{a \times \exp[(x_0 - x)/b]}{b \times (1 + \exp[(x_0 - x)/b])^2} \quad (2)$$

In analogy to physics,  $dy/dx$  in Eq. (2) can be viewed as acceleration in the temporal progress of epigenetics. The plot of  $dy/dx$  as a function of  $x$  (time in years) visualizes a long-term projection of the development of epigenetics (Fig. 1D).

In addition to the quantitative analysis, the importance of epigenetics can be assessed based on its position in the science hierarchy. The history of science shows that there is a directional effectiveness in science (Fig. 2A) (15). An examination of publications in epigenetics allows us to build a similar hierarchical structure focusing on epigenetics based on the operational level and explanatory power of the subject (Fig. 2B). In the proposed structure, chemistry is fundamental to the research of epigenetics as it provides essential tools for the research (16). It also shows that epigenetics can be applied to numerous fields, such as nutritional sciences (17–20), environmental sciences (21), and psychology/psychiatry (22–27), in addition to traditional biological sciences (for example, 28). The unique position of epigenetics linking several different subjects in the hierarchical structure provides another justification for including this discipline in undergraduate curriculum. It will be particularly useful in the career development of biology undergraduates, as they can apply knowledge acquired from epigenetics courses to advanced graduate study in fields such as nutritional sciences, environmental sciences, or psychology/psychiatry, where the concept of epigenetics is rapidly expanding.

In our previous paper (12), we discussed the value of teaching resources including textbooks for effective education. We believe that should be the case for epigenetics as well. Here we introduce several resources that may be useful for educators as well as students. Currently, there are several books on epigenetics published for the general public (29–35) or more academic audiences (36–39). Among

those books, we found that *The Epigenetics Revolution* (30) was suitable for students of biological sciences (40). In addition, there are several online resources available. A compiled list of multimedia teaching resources can be found in Stark's paper (41). Additional online resources for science educators include Nature's Spotlight on Epigenetics (<http://www.nature.com/scitable/spotlight/epigenetics-26097411>), the Plant Cell's premade PowerPoints, handouts, and lecture guides (<http://www.plantcell.org/content/ttpb4>) (42), and Epigenesys's website, which offers a compilation of teaching resources (<https://www.epigenesys.eu/en/>).

Regarding the structural format of an epigenetics course, we suggest two options: it may be taught as a stand-alone course, or it can be incorporated as a component in other related courses such as genetics or cell biology. In either case, we propose three themes be included in the teaching of epigenetics: principles, techniques, and applications of epigenetics as suggested in *The Epigenetics Revolution* (30, 40). We expect that the books, some of the review articles, and the online resources listed in the references of this paper can be used in teaching the principles of epigenetics. In addition, an issue of the magazine *The Biochemist* (<https://portlandpress.com/biochemist/issue/39/5>) that focuses on epigenetics should be a valuable resource. If one is interested in the physics of epigenetics, a recent article (43) will be a valuable source. Regarding techniques, we suggest that educators consider including two particular techniques, chemistry, explained in Volume 115, Issue 6, of *Chemical Reviews* (<https://pubs.acs.org/toc/chreay/115/6>) and bioinformatics (44–46), which considers the nature of epigenetics.

## CONCLUSION

In summary, epigenetics is a rapidly emerging biological science. Its academic importance is expected to reach 20.7% of genetics in ten years (year 2029). The position of epigenetics in the science hierarchy suggests that it has the potential to serve as an interdisciplinary subject. Diverse teaching resources for epigenetics are already available. For all these reasons, we suggest the academic community include epigenetics in their curricula.

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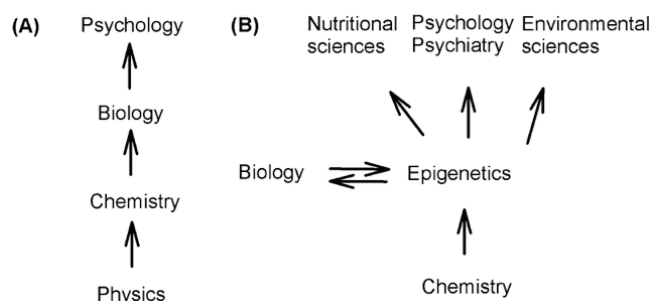


FIGURE 2. Standard hierarchical structure of sciences (A) and a hierarchical structure including epigenetics (B).

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