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Pulling the Plug on Microscopes in the Anatomy and Physiology Laboratory

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Abstract

Virtual microscopy (VM) has been widely available for more than a decade, especially in clinical settings and medical schools. In recent years the movement away from conventional optical microscopy (OM) and towards VM has been accelerating and several VM websites are now available online and readily accessible to educators. VM can enhance the instructor's ability to teach the histology component of anatomy and physiology classes, facilitate student learning, save time for both students and instructors, and ultimately save money that can be more productively used for other facets of the laboratory. The many pedagogical and practical advantages provided by VM suggest that now is the time for undergraduate anatomy and physiology programs to consider a transition to VM. doi: 10.21692/haps.2017.024

Key words: Histology, Virtual Microscopy, Educational Technology, Paradigm Shift, Digital Imaging

Introduction

Histology is a central part of the human anatomy and physiology laboratory curriculum. It reveals the microscopic structure of organs and tissues, elucidates the connection between structure and function, provides an understanding of the underlying chemistry through selective staining, and enables the comparison of normal and pathological tissues. For over a century, undergraduate lab work in histology was synonymous with the use of optical microscopes and glass slides. Learning how to focus, view different planes, adjust the light, and pan over tissue sections was a rite of passage for those entering health-related fields.

In conventional histological lab work, researchers and students look through an optical microscope at a tissue suitably mounted on a glass microscope slide. In this fashion, the practice of OM continues a pattern of research and learning that was begun several hundred years ago with Antonie van Leeuwenhoek's hand-produced microscopes and Robert Hooke's identification of "cells." The identification of plant cells by Matthias Jakob Schleiden and animal cells by Theodor Schwann, as well as the pioneering work by microbiologists, were all made possible by the powerful ability of the optical microscope to expand our vision to see structures that were too small to see using the naked eye. High school and general college biology courses have long emphasized the use of optical microscopes to study suitably prepared specimens mounted on glass slides.

Increasingly, however, the OM tradition is being replaced by virtual microscopy (VM). In VM, high-resolution digital files are created by digitally scanning high quality tissue specimens mounted on glass microscope slides. The digitized information is stored on a server in a manner that allows users to access the digital image, and to search (pan) and magnify the image just as with OM. Focusing in multiple image layers and across different focal planes can also be carried out using appropriate technology. Multiple users can access images simultaneously via the Internet if VM data is set up on a web-based platform.

Virtual microscopy images often exceed the viewing quality and resolution of the best optical microscope and glass slide combinations. It must be emphasized that VM is very different from conventional photomicrography, in which static images are created using a camera to take a photograph through a light microscope, e.g. the images found in textbooks, lab manuals, and histology atlases, as well as on PowerPoint slides or in videos. Such static images, which cannot be manipulated by the user, do not meet the definition of virtual microscopy (Wilson *et al.* 2016).

Virtual microscopy has been widely available since approximately 2005 (Ogilvie 2005, Scoville and Buskirk 2007), especially in clinical settings and in medical schools, where funds for the needed technological changes are more readily available than in two-year and four-year undergraduate colleges (Wilson *et al.* 2016, Vainer *et al*. 2017). The movement towards VM has been accelerating, and several VM websites are now available online and readily accessible to educators. The generally superior quality and improved access provided by VM suggests that now is the time for undergraduate anatomy and physiology programs to consider a transition from OM to VM.

Moving from optical to virtual microscopy

The histology portion of anatomy and physiology labs has long been a comfortable technological backwater, isolated from the rush of technology. Optical microscopes have improved somewhat in the past fifty years as advances have been made in technology including a shift from monocular to binocular, adding a mechanical stage, incorporating in-base lighting, facilitating two-person viewing, and adding digital and projection capabilities. However, these incremental advances have not had a significant impact on the learning experience of the typical undergraduate student in the histology portion of the anatomy and physiology lab. At many colleges, a student's exposure to histology in the

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second decade of the twenty-first century is little different than the experience of a comparable histology student at the end of the nineteenth century.

Increasingly, however, individual instructors and entire departments have experimented with modifications to the traditional presentation of histology in the laboratory. At least one college completely replaced OM in its anatomy and physiology classes with high quality photomicrography viewed on computer screens. This decision was based on considerations of pedagogy, efficacy, and cost (Hubley and Zeigler 2013, Hubley 2017). The present authors have experimented with using digital devices (e.g. tablet computers), along with a histology software application, either in concert with or instead of OM. We have found that this approach was effective in motivating anatomy and physiology lab students to learn the subject matter (Ostrin and Dushenkov 2016) (Figure 1).

Figure 1. Students using digital images, rather than a microscope, to study tissues. Digital technology is effective in motivating anatomy and physiology lab students.

The past decade has seen exponential growth in the number of digital microscopy applications in research and medicine, a phenomenon that is illustrated by the explosive increase in the number of articles published in this field. This trend is mirrored by a similar increase in the number of articles describing the use of digital microscopy in education and the implementation of VM in medical schools (Figure 2). Many departments and institutions have replaced OM with VM in the histology laboratory. The rapid decline of OM is particularly apparent in medical schools, although it is not clear what percentage of institutions in academia or the allied medical fields have shifted from OM to VM. Large universities in the United States, including the University of Michigan (Hortsch 2013), University of Iowa, NYU, and Duke University, have taken the lead in adopting VM technology, citing the obvious pedagogical, efficient, and financial advantages of VM.

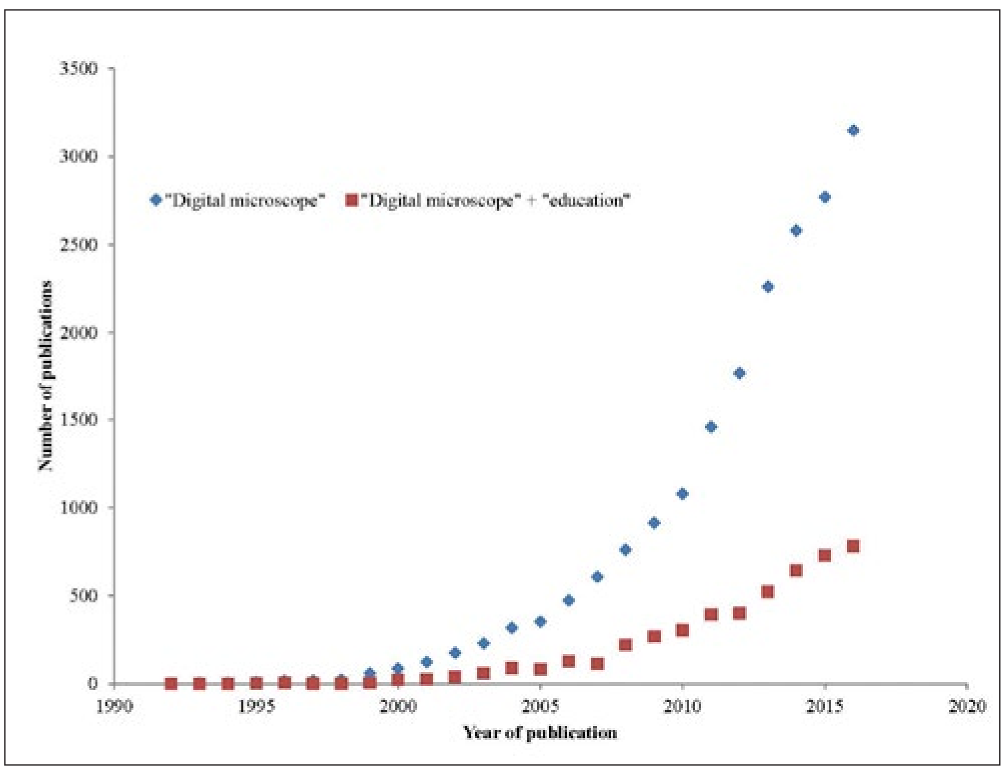

Figure 2. Graph represents the results of a search in Google Scholar (scholar.google.com) on July 13, 2017 to find journal articles from the years 1990-2016 that contain the following search terms anywhere in the article: (a) the exact phrase "digital microscope"; (b) the exact phrase "digital microscope" combined with the word "education."

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Numerous studies, albeit almost exclusively in medical schools, indicate the pedagogical equivalence or superiority of VM to OM in teaching histology and pathology. When the Medical College of Wisconsin converted two of its first-year courses, in cell and tissue biology, and in integrated medical neuroscience, to VM, a survey of students and faculty indicated that VM was very favorably received. Examination scores in courses where students used VM were comparable or superior to courses where students used OM (Krippendorf and Lough 2005). A study of students taking histology at Eastern Virginia Medical School found no significant difference in the test scores of students using VM and students using OM (Scoville and Buskirk 2007).

At the University of Turku, Finland, a comparison of the test performance of medical students taking pathology classes using either OM or VM gave mixed results. Although the VM group had superior test results for normal histology, the OM group had superior results for pathological histology (Helle *et al.* 2013). At Ghent University, Belgium, there were no significant differences in the test performance of medical students studying histology using either VM or OM (Mione *et al.* 2013). At the Third Military Medical University in Chongqing, China, test scores of students using VM were significantly higher than the scores of students using OM (Tian *et al.* 2014). The School of Medicine at the University of Barcelona, Spain, found no difference in knowledge among medical students studying pathology by either VM or OM (Ordi *et al.* 2015).

A meta-analysis by Wilson *et al.* (2016) combined the outcomes of twelve studies that compared the effectiveness of OM and VM. The students in the studies were mostly medical students or college undergraduates in either histology or pathology lab classes; 1,978 of the students were in classes that used VM, and 3,950 students were in classes that used OM. The meta-analysis pointed to the pedagogical effectiveness of VM, indicating that the use of VM in the lab had a small but statistically significant positive effect on student learning. Furthermore, students "reported a general preference, or favorable attitude, toward VM over OM." The authors suggest that improvement in learning may be attributable to both the "ease of access" and "ease of use" of VM over OM (Wilson *et al.* 2016).

Implementation of VM has become commonplace and generally accepted. In the Fall of 2016, when the University of Copenhagen Faculty of Health and Medical Sciences phased out its use of OM and replaced it with a new automatic VM system, it did not make an effort to compare the pedagogical efficacy of VM and OM, but merely surveyed its users, and reported that the VM system "has been received positively by both teachers and students" (Vainer *et al*. 2017).

Clinical studies have also shown the efficacy of VM when compared to OM (Ho and Pantanowitz 2017). One clinical study, which used guidelines of the College of American Pathologists to analyze pediatric surgical pathology and cytopathology cases by OM and VM, found that VM was sufficient to adequately review pediatric surgical pathology specimens. The study concluded, however, that the VM review of pediatric cytopathology specimens was less successful and would likely require additional "capture in multiple focal planes" (Arnold *et al.* 2015). Similarly, when six pathologists used VM and OM to analyze microscopic features seen in dermatitis, they found that VM was sufficient to identify histopathologic features, although it took less time to evaluate cases using OM (Vyas *et al.* 2016).

Some European countries already accept VM pathology diagnosis. For example, hospitals in the Netherlands and Sweden have replaced OM with VM for diagnostic purposes. The Copenhagen University Hospital (Rigshospitalet) pathology department, which produces more than 800,000 glass slides annually from 95,000 tissue samples, expects to completely replace OM analysis with a VM system by 2020 (Vainer *et al*. 2017).

On April 12, 2017, for the first time, the U.S. Food and Drug Administration approved a proprietary VM whole slide imaging (WSI) system that will allow pathologists to "to read tissue slides digitally in order to make diagnoses, rather than looking directly at a tissue sample mounted on a glass slide under a conventional light microscope." The FDA approval came after a clinical study of approximately 2,000 pathology cases, which found that diagnoses made using the approved VM system "were comparable to those made using glass slides." The FDA noted that the risks associated with VM are similar to those of using conventional OM (Food and Drug Administration 2017).

The digital microscope provides much more information than a conventional microscope, even if the latter has a digital camera. The digital microscope can automatically capture images on several fluorescent channels and on a transmission light channel. It can also stitch together intermediate images and obtain a large area image in high resolution, as well as capture full-focus images of thick objects. The combination of these two options in VM allows complete information to be obtained about the 3D structure of the object.

Benefits of virtual microscopy in the anatomy and physiology laboratory

Microscopy typically occupies a significant amount of time in most anatomy and physiology laboratory periods. In our college, three of the fourteen anatomy and physiology I lab periods are devoted exclusively to microscopy. There is one lab in which students learn how to use the microscope, and two labs in which students study the four tissue types and the integumentary system. Most of the other labs in anatomy and physiology I and anatomy and physiology II contain additional lab segments devoted to examining the tissues of specific organ systems. This heavy emphasis on microscopy is probably the same in most college-level anatomy and physiology courses.

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However, despite the many hours that students spend in the anatomy and physiology lab using OM to learn histology, the general consensus in our department is that our students get very little productive learning out of the time and effort that they devote to this endeavor. The reasons for this state of affairs are manifold. Large lab class sizes prevent personalized instruction, the many variations among the slides of a single tissue cause confusion, unfamiliarity with the microscope and how to focus it can be frustrating, and the lack of access to microscopes and slides outside of scheduled lab class means that students cannot study the slides on their own.

Student difficulties with OM are not limited to community colleges or pre-nursing anatomy and physiology courses. The same problems appear among students at major universities. For example, at the University of Copenhagen Faculty of Health and Medical Sciences, prior to converting to VM, teachers in the histology and pathology labs often had to provide one-to-one instruction at dual-head microscopes, which "demonstrated that many students were unable to obtain an image on their microscope and also found it difficult to locate relevant areas on their slides" (Vainer *et al.* 2017).

If we weigh the importance of each lab class hour, and the mass of material that must be taught, understood, reviewed, and mastered, against the *de minimis* productive learning that most students get from their lab time and effort when using OM, the question that should naturally arise is whether OM and glass slides are necessary in the modern, twenty-first century anatomy and physiology lab. Are the OM skills that we try to instill in our anatomy and physiology students intrinsic to studying histology, or are these skills a distraction and irrelevancy in today's anatomy and physiology lab? The thesis of this article is that VM, while not a panacea for all the ills of the anatomy and physiology program, can enhance an instructor's ability to teach histology, facilitate student learning, save time for both students and instructors, and ultimately save money that can be more productively used for other facets of the lab, e.g. physiology equipment.

VM has been shown to be pedagogically sound. Overwhelmingly, studies of OM vs. VM learner performance and preference substantiate the pedagogical efficacy of teaching with VM, which is at least comparable, and in many cases superior, to OM. The earlier cited meta-analysis showed that VM demonstrated "small yet significant positive effect on learner performance . . . indicating that learners experience marked knowledge gains when exposed to VM over OM . . . An analysis of trends in learner perceptions noted that respondents favored VM over OM by a large margin (Wilson *et al.* 2016). Other studies reported in the literature attest that histology labs using VM were not disadvantaged pedagogically, and histology students generally preferred VM to OM. Additionally; it has been shown that digital technology improves student interest and attention (Ostrin & Dushenkov 2016).

Time and place constraints evaporate when a VM setup is made available to students on the Internet. Access to the histological images is not limited to specific lab hours or specific lab rooms. Students can study the slide images whenever and wherever they want, providing true open access and eliminating any need for "open lab" study time. Several studies reported "strong majorities of students (80.7% - 93.8%) who believed that VM saved them time compared to using the optical microscopes" (Wilson *et al.* 2016). Additionally, VM may well be beneficial for students with accessibility issues, including vision or physical conditions that make it difficult to use an optical microscope.

Virtual microscopy has the potential to eliminate the steep learning curve inherent in OM. VM reduces, even if it does not eliminate, the frustration that many students have when using OM. Today's students come to VM already comfortable with the mundane technologies of the twenty-first century, i.e., computers, software, and the Internet. In contrast, the optical microscope, with its glass and metal parts, and its manual adjustment knobs, is arcane and unfamiliar. Many anatomy and physiology students never fully master the complex skills involved in OM such as focusing on a single or multiple planes, adjusting the light, or panning over different areas of the slide. In the typical anatomy and physiology histology lab using OM, weaker students waste valuable lab time looking at unfocused images, the wrong area of the glass slide, or a slide in which the sectioning and staining are inadequate. It is impossible for instructors in large lab sections (we have up to twenty-eight students in our anatomy and physiology labs) to help every student who has OM problems. Consequently, by the end of a typical OM histology lesson a large percentage of students have not mastered what they were supposed to see or learn during the lab period.

Switching the histology lab segment from OM to VM can save lab time that is better used for other purposes. It will enhance the instructor's ability to present core principles, and can free up lab time for recitation and student-centered activities that enhance learning, such as self-study, group-work, peer-teaching, collaborative education, and team-based learning. VM images can be presented in both labeled and unlabeled versions for student self-study online. The VM images can have explanatory text added, and can be further used in digitized in-class or on-line histology exams and for on-line learning. These options facilitate more uniform and comprehensive lab instruction. Newer instructors, who may be less familiar with the intricacies of histology or the manner in which it is taught in a specific program, will be able to prepare their lessons more effectively.

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Arguments against using virtual microscopy in the anatomy and physiology laboratory

Those who argue against implementing VM present two main reasons for retaining OM in the anatomy and physiology laboratory:

1. Optical microscopy is superior in preparing students for future OM coursework and clinical practice.

2. Optical microscopy is pedagogically superior to VM.

Let us examine these claims.
The first claim suggests that OM experience in anatomy and physiology is needed to prepare students for future OM coursework. Indeed, although students majoring in biology or taking microbiology have a real need for OM skills, particularly if they will be doing fieldwork, they can acquire their OM skills in other biology courses. Many students who take anatomy and physiology have already been exposed to OM in prior course, or are in programs (e.g. radiation technology) that either do not have a microbiology requirement or allow students to take microbiology concurrently with anatomy and physiology. In such cases, the anatomy and physiology lab time spent on OM training is superfluous. Furthermore, instructors at our school report that many superior students who reach microbiology after two semesters of anatomy and physiology still have not mastered the optical microscope. A good argument can therefore be made that the microbiology lab is the best place to teach OM skills, especially those skills particularly relevant to microbiology, including high power focusing and use of the oil immersion lens (a skill that is often not taught in anatomy and physiology).

The first claim also suggests that OM skills will be needed after students graduate and enter the professional world. In our own institution, it is not clear that our students, who primarily train to become nurses, dental hygienists, or X-ray technologists, will have a need for OM skills in their professional careers. The conventional optical microscope is largely not used in medicine and related fields, at least in the United States and Europe. Even in places where it is still being used, OM is being rapidly phased out in favor of VM. Lab tests formerly carried out using OM have long been replaced by automated equipment. For example, in pathology the trend is toward VM or to artificial intelligence (AI). For those professions other than medicine (e.g., veterinary science) that may require proficiency in OM, the microscopes that graduates will encounter on the job will be different than the kinds of microscopes found in undergraduate classrooms, and therefore on-the-job training will be needed.

The second claim suggests that OM is pedagogically superior, because it involves hands-on contact with "real" variable tissues and requires students to focus slides and discover appropriate structures, whereas VM shows only "idealized" pre-focused images of tissues and not the real thing, thereby depriving lab students of contact with actual bits of tissue. According to this line of reasoning, OM provides students with a richer pedagogical experience and a better understanding of cells, tissues, and organs than can be achieved with VM. However, the literature indicates quite the opposite; namely that VM is pedagogically superior to OM as a means of teaching students about tissues. As noted earlier in this paper, student grades on histology tests are higher in classes where students learn with VM. This outcome is not surprising when one considers that VM permits students to learn histology at "any time" and "any place" (Wilson *et al.* 2016, Hoar 2017), and minimizes most of the frustration and inefficiency of OM. Since OM images and VM images come from the same source, a preserved and stained bit of tissue mounted on a glass microscope slide, there is no greater "reality" inherent in the OM image when compared to the VM image, and there is no evidence that students get a richer experience by using OM.

Students are comfortable with digital imagery, understand its provenance, and readily understand the relationship between glass microscope slides and digital images (Figure 3). Both OM and VM enable the user to change the field of view and the magnification, although of course this operation is more easily done in VM. The variability of normal specimens of the same tissue, as well as comparisons between normal and pathological specimens, can be demonstrated in both OM and VM, though more easily in VM. Focusing is the only operation that can be readily done in OM, but is not generally available in VM as presently constituted. However, since focusing is one of the most problematical aspects of OM for anatomy and physiology students, the fact that VM images are always in sharp focus makes the student's VM histology experience more productive than OM.

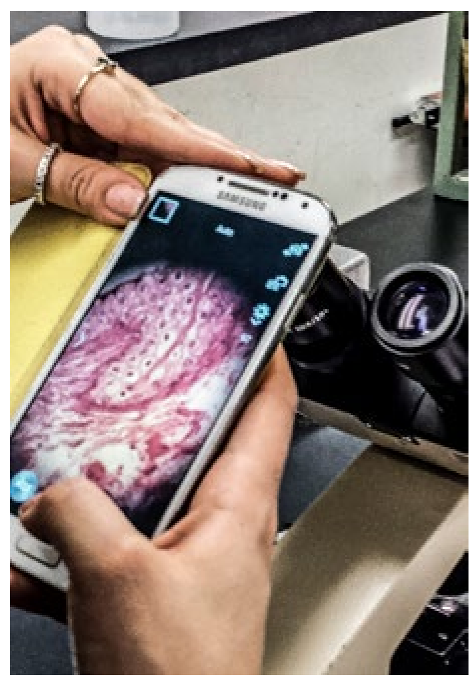

Figure 3. Student using a smartphone to capture a digital image through an optical microscope. Students are comfortable with digital imagery, and understand the relationship between glass microscope slides and digital images.

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It is critical that we do not lose sight of the underlying purpose of the histology segments in the anatomy and physiology lab, namely to help students gain an understanding of the micro-anatomy of human tissues and organs, and to connect that understanding to normal and abnormal human physiology. In today's technological environment, VM is the superior tool for anatomy and physiology instructors charged with teaching histology, and for students who must acquire this knowledge. At the University of Wisconsin-La Cross, OM was replaced by VM in the undergraduate anatomy and physiology labs in 2011. Some instructors were "a bit skeptical" when VM was first implemented, but currently there is a consensus that the conversion to VM has been a success (Hoar 2017). Students taking anatomy and physiology courses at the University of Wisconsin-La Cross can now study histology whenever and wherever they want, and indeed, they tend to do most of their studying for histology outside of the lab, and use their lab time to study specimens and models that are accessible only in the lab room. Test scores on anatomy and physiology exams that emphasize histology increased after the university switched to VM (Hoar 2017).

Converting to virtual microscopy

Once a decision is made to convert the anatomy and physiology labs from OM to VM, there are several issues that need to be addressed, specifically regarding the technical and financial aspects of implementing the new VM technology as well as pedagogical issues that pertain to the use of VM by instructors and students.

Each student in the lab would need access to a computer, either provided by the school or obtained by the student, in order to permit individualized access to the VM images during the lab period. In principle, a regular lab room would not be required for VM work, since computer carts containing a full set of laptops or tablet computers could be moved to any classroom, as long as the room had a projector that the instructor could use to show the class enlarged VM images. Outside of the lab period, of course, students would be able to access the VM images on any of their own digital devices. The institution would need to upgrade Internet and Wi-Fi connectivity to a level that would permit multiple lab sections to have simultaneous high-speed access to the high-resolution VM images. Although the purchase of computers and upgrading Internet and Wi-Fi will incur a cost, the benefit is that there will no longer be a need to service or replace optical microscopes.

VM images, stored in folders called "digital slide boxes," are freely available to faculty and students over the Internet from a number of academic institutions, including the University of Michigan. Textbook publishers are also getting involved in providing VM resources. Alternatively, a college can create its own customized digital slide boxes from an existing collection of tissue slides. The scanning process, conversion into a digital format, and provision for storage and retrieval can be carried out by the college itself, or by a commercial service that will take responsibility for these steps. Going forward, one can envision a consortium of colleges that would pool their existing glass slide collections into VM format with free access by all of the colleges and their students. In April 2017, a version of such a consortium, the Virtual Microscopy Database (VMD), was launched, and designed as a free resource for researchers and educators, but not students (Lee *et al.* 2017).

The greatest challenge involved in the transition to VM will likely come from the pedagogical aspect. Instructors will need to become familiar with the new VM images, the web locations of the images, and the VM interface. Instructors will need to modify their teaching and lab presentation in order to take full advantage of the power of VM. The time freed up by not needing to explain the care and the operation of an optical microscope, or to help individual students with lighting, focusing, etc., will now be available for more productive pedagogical purposes. Online and hardcopy instructional materials, as well as lab quizzes on histology will need to be revised in order to reflect the use of VM in the lab.

The above changes do not have to occur simultaneously. A department can start slowly, buying one set of computers, setting up one lab room at a time for VM, using freely available VM images initially before deciding whether to create a customized digital slide box, and modifying the pedagogy in increments. In the end, all of the foregoing changes should be seen as evolutionary, not revolutionary. The changeover from OM to VM can be seen as merely a change in "operating system" or "platform," since bits of stained tissue on glass microscope slides, which are magnified by some form of optical microscope, form the histological basis for both OM and VM. In OM the glass slide is directly viewed, whereas in VM the image is first stored in a digital format before being viewed.

Conclusion

Although the conventional optical microscope was necessary for viewing histological preparations in the anatomy and physiology lab prior to the current digital age, the manifold advantages of virtual microscopy (VM) in terms of access, use, pedagogy, and cost make it the clear choice today. The movement away from conventional optical microscopy (OM) and towards VM in both the professions and academia has been accelerating. Numerous VM websites are now available online and readily accessible to educators and students. The generally superior quality and the many pedagogical advantages provided by VM suggest that now is the time for undergraduate anatomy and physiology programs and lab instructors who have not yet made the switch to consider and indeed plan transitioning from OM to VM.

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