

New Tools for Physiology

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Physiology 23:234, 2008. ;

doi: 10.1152/physiol.00021.2008

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Historically, the subspecialties of natural sciences developed on the basis of the application of novel methods that allowed new approaches and opened new horizons of understanding. In fact, physiology developed from anatomy (e.g., the first physiological chair in Berlin, Germany was established in 1853 and held by Emil Du Bois-Reymond, who originally had an “anatomic laboratory”) as soon as new methods made it possible to study function beyond mere morphology. In the beginning, it was mainly the understanding of “electrical phenomena,” for which physics had just delivered new tools. The application of the new methods in living tissue and animal models formed a monopoly: new or unsolved questions met the methods that promised to solve them, and, due to intensive research, new special areas developed. This pattern repeated itself over the years, leading to the birth of biochemistry and molecular biology. However, the new methods no longer “belong” to one single subspecialty but rather form the arsenal of any of the biological and medical natural sciences. Molecular biology, (epi)genetics, protein chemistry, and analytical work at the cellular level have become common to all of them. No longer, therefore, do any of these sciences have unique features when it comes to the methods dissecting cellular signaling cascades or the function of genes. From this point of view, some may go as far as to argue that the continuation of any subspecialty has become unnecessary and in fact “life sciences” or, sometimes more organ-specific neurosciences or cardiovascular sciences seem to be on their way to replace them. As a consequence, in some countries, physiological institutes have

been closed and made part of organ-related life science programmes or molecular biology divisions.

Does this mean that there is no future for physiology as such? Physiologists insist that, in addition to analyzing molecular signaling processes and genetics, it is necessary to understand the complexity and apparent redundancy of signaling processes. Physiologists insist on understanding the functional interaction of cells—as well as their coordination by the vascular system, hormones, and nerves—to get a real picture of organ function and, eventually, the processes leading to diseases. The analysis of this intricacy, be it at the cellular level or beyond, was always a true physiological domain . . . and is true now more than ever. For example, the development of transgenic animals with unexpected phenotypes has given new insights into the complex pathways of signaling events, receptors, and factors in a whole organism and the compensating capacity and redundancy of systems.

What a chance if this complexity could be studied with new tools that support the genuine “physiological approach”! In my view, the rapid progress of bioimaging methods offers such tools and opportunities and should be grasped eagerly by all physiologists. One example is two-photon microscopy, which permits study of the interaction of cells inside intact tissues. Luminescent gene products, new cell-tracking methods, and other approaches offer further novel ways to study gene expression and other dynamic events in cells in their natural environment. And, most importantly, the application of PET and MRI offer new and unique ways to understand, for example, blood-flow regulation, metabolism, and receptor expression in

the intact tissue without even touching the animal. Higher field strengths in MRI together with analytical mathematics allow resolutions that now extend almost to the level of single cells. I am confident that such imaging approaches will lead to a revolution in the understanding of integrative mechanisms in living tissue. “Systems biology” has become a hot subject. In fact, an important subarea within systems biology is really integrative physiology. Focusing at the organ level and beyond, integrative physiology will rise to new levels of sophistication and, I believe, will rival the understanding of complex signaling within a single cell. In fact, these two approaches—systems biology at the levels of integrative physiology and cellular biology—will support each other and offer insights of which the current generation of physiologists can only dream. A new generation of physiologists needs to be trained to understand and develop these possibilities further with regard to the questions they have in mind. Moreover, a more general involvement of physiologists in the further development of the aforementioned new techniques will also involve them automatically more into translational medicine. It is my firm belief, supported by the German tradition in which physiology was always in the center of medical progress, that translational medicine is unthinkable without physiology. So far, people working on high-field MRI have shown us wonderful anatomical pictures of the brain and other organs with an unheard of resolution; “intravital morphology” of the highest anatomical standards can be observed. At this point, physiologists should not wait too long to become again “independent” of morphology as they already did 160 years ago. Physiologists must take the lead and work actively in their universities to make these wonderful tools available for physiological questions and thus help to develop them further. ■