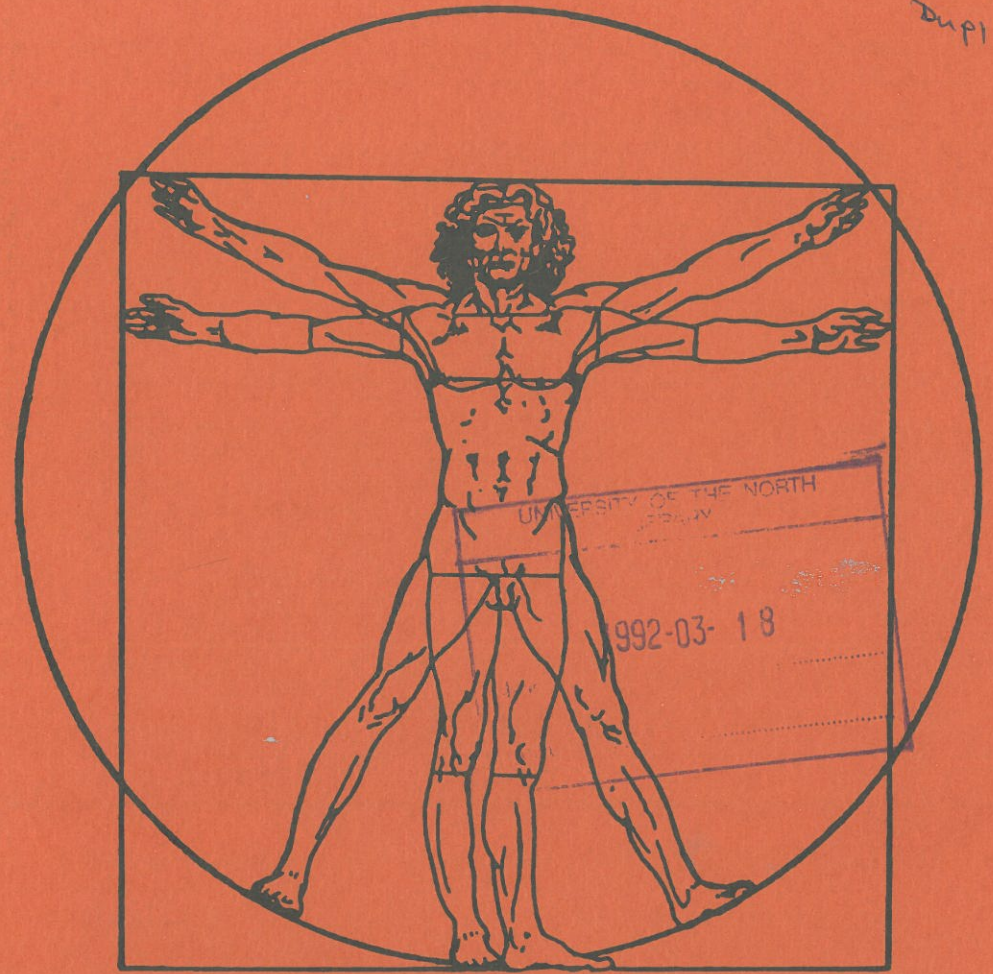


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**THE MODERN PHYSIOLOGIST:  
BUTCHER, BAKER OR  
CANDLESTICKMAKER?**

AN INTERDISCIPLINARY APPROACH TO PHYSIOLOGY

**WILLEM J. ELS**

M.Sc. (Illinois) D.Sc. (Stellenbosch)

# THE MODERN PHYSIOLOGIST: BUTCHER, BAKER OR CANDLESTICKMAKER?

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INAUGURAL LECTURE DELIVERED ON ACCEPTING THE CHAIR OF  
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ON FRIDAY, 2ND MARCH 1979.

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## INTRODUCTION

Mr. Chancellor, Mr. Rector, members of the Council, colleagues, ladies and gentlemen:

Historically the biological sciences were organized in universities according to the organism of interest. The usual disciplines thus organized were botany, zoology, medicine and veterinary medicine. Most physiology departments appeared in schools of medicine but since the University of the North does not have a school of medicine, physiology was first offered in the department of Zoology. In 1970 the independent department of Physiology was established, and its resorts under the Faculty of Mathematics and Natural Sciences.

Since physiological principles are fundamental to the analysis of living systems, its study is an integral part of many biological and medical disciplines. By virtue of this common interest physiology has strong academic ties with a number of disciplines in both fields as, for example, biochemistry, animal physiology, pharmacology, clinical medicine and pathology. At the University of the North we offer a number of courses in physiology to students of Natural Science, Pharmacy, Nursing, Optometry and as from next year, Pathology. With the further development of the University it is foreseeable that additional demands for physiological study could come from fields of study such as veterinary science, physical education or other paramedical sciences.

\* \* \*

It is my intention this evening to explain briefly what modern physiology entails, especially in the light of recent advances in other sciences. Since the field of physiology is wide and dynamic, the image of the physiologist is constantly changing. The physiologist has the habit of turning up in unexpected situations and biographies of famous scientists in fields of medicine, veterinary sciences and biology, often reveal that by training they are in fact physiologists. Pavlov, the famous Russian physiologist had for many years before held the chair in pharmacology at the Military Medical Academy in St. Petersburg. In recent years it has become not uncommon to have electrical engineers or computer scientists address physiologists at meetings, and for physiologists to address engineers at their meetings. Hence, to many of the public (and probably to some of my colleagues) the activities of the physiologist must seem like those of the alchemists of old — obscure and mysterious.

## THE FIELD OF PHYSIOLOGY

Since physiology has meant different things at different times, it is perhaps a sound policy first to define the subject under discussion as precisely as possible. The term physiology comes from the Greek word *physis* which, loosely translated, means 'nature'. Unfortunately even the word 'nature' is

an ambiguous one, but in its modern context physiology may be defined as the area of science devoted to analyzing the normal events and activities of living systems.

Unfortunately physiology defined and physiology as taught by University departments are often two different things. Probably because the majority of Physiology Departments are attached to schools of medicine the emphasis has always been on the physiology of man. Since, however, research is commonly done on other animals, most Physiology Departments are in fact committed to the teaching of vertebrate (especially mammalian) physiology. The physiology of other organisms is then usually studied in other Departments, as, for example, Zoology. Because of this division of interest it is imperative that physiologists should not lose sight of the fact that their field of study is analysis of the events and activities fundamental to *all* living systems. Granted that the advance of medical science might justify a special interest in mammals, but much of our understanding of the fundamental problems may come from the study of lower forms. Prof. A.C. Burton<sup>1</sup> has said very cogently and very truly:-

"What does he know of mammals, who only mammals knows?"

In this regard one of the most useful, but often neglected biological concepts is the August Krogh principle which states that for many physiological problems there is an animal on which it can be most conveniently studied.<sup>2</sup> Hans Krebs has emphasized the importance of deliberately searching for the right experimental material when attempting to tackle specific problems in biological and medical sciences.<sup>3</sup> Often in human and medical science spectacular advances have been made only after selecting the right animal for the experiment. Prosser<sup>4</sup> has pointed out that the highly specialized functions of invertebrates may eventually provide the ideal material for the study of many problems in bio-medical research, especially at cellular level. So, for example, Willows found the nudibranch *Tritonia* the ideal animal for the study of brain cells, while the pioneering studies by Hodgkin and Huxley on the nerve physiology of the squid is perhaps the best-known example of this principle. Similarly the frog skin has proved to be the ideal model to use when studying the active transport of sodium across epithelial cells.

### PHYSIOLOGY AND COMPLEXITY

The study of physiology is a very complex one, partially because the living systems which it deals with are in themselves very complex. Consider only the wide array of functional phenomena found in organisms, or the range of organizational levels open to study — from whole animal through organ, tissue, cellular, subcellular, molecular to atomic levels — then an appreciation of the extent of the complexity appears. The complexity in physiological research is also an inevitable consequence of modern laboratories. With the tools now available to the scientist it has become possible to analyze cellular events at molecular level. Especially the advances in electronics since the second World War have made a wide

range of investigations possible, such as recording bio-potentials from single cells, or even parts of cells.

Historically there was the idea that there was a *vital* difference between living and non-living matter, and it was further thought that the nature of the chemical components of living matter differed from those of non-living matter. These ideas have since been dispelled as erroneous. Living systems are composed of the same atoms and molecules as non-living ones and hence are subject to the same laws. Basic phenomena in physiology and other life sciences are now being described in terms of the natural laws governing matter. There are, however, certain quantitative differences between living and non-living systems.<sup>5</sup> Living systems have many more components which are more closely connected than non-living ones, and there are thus greater problems in analyzing the principles of a living system in terms of all its component parts. Opponents of the molecular approach to the life science may thus argue that the living system has too many different things going at one time, and when taking them apart to study the relative simple components one may be breaking important connections. But the same problem applies to complex non-living systems: if, for example, you are faced with the problem of understanding any complicated electric circuit without a wiring diagram, your conceptual problem will be similar to that facing the physiologist in trying to analyse the functioning of an organism.

### THE INTERDISCIPLINARY NATURE OF PHYSIOLOGY

For over a century many important contributions to the life sciences have come from chemistry and physics. Lately, especially since Physiology has emerged into the realm of molecular science, living systems are profitably analyzed by the exponents of basically non-living systems. Hence, many contributions to our current physiological knowledge have come from physicists, mathematicians, physical chemists, engineers and others. While there has always been a close association between physiology and the chemical sciences, it is only comparatively recently that the barriers between physiology and the physical sciences have been broken down. Many of the earlier contributions from the physical sciences were done under trying conditions.

Von Békésy, a physicist from the University of Budapest, has made valuable contributions to the understanding of the physiology of acoustics. While an engineer for the Bell telephone company he became interested in the mechanical properties of the human ear, which he compared with the telephone membrane. He naturally wanted to perform his experiments on the human ear but met with opposition from the anatomy professors since at the time the general feeling was that physicists should not become involved with biology.<sup>6</sup> Fortunately this strict division between the physical sciences and the life sciences has since disappeared and the study of physiology has taken on an interdisciplinary approach. In 1961 von Békésy, although a physicist by training, received the Nobel prize in Physiology and

Medicine for his work on acoustics. At his death in 1972, he was a Professor in Sensory Sciences.

The interdisciplinary approach to the life sciences has brought about many important changes in physiological study. Amongst these is the fact that the physiologist now has new tools for research at his disposal. At the turn of the century the physiologist Etienne Marey made a prophetic statement:

"In the field of rigorous instrumentation, all sciences give a hand. Whatever the object of these studies, that which measures a force or movement, or electrical state or temperature, whether he (the investigator) be a physicist, chemist or physiologist, he has recourse to the same method and employs the same instrument."

Thus it is that recent advances, especially in physical technology, have greatly benefited physiological research by bringing about new experimental approaches. During the development of the American space programme there was an especially rapid development in the electronics industry which, indirectly, contributed greatly to our physiological knowledge. In this respect it is only necessary to recall the impact the development of the computer system had on biological research. Similarly the development of the monolithic integrated circuit greatly influenced physiological experimentation. A wide range of high input impedance amplifiers is now commercially available to measure biological potentials very accurately. By using integrated circuits it is possible, even for non-specialists, to construct electronic systems for a particular investigation to a degree of complexity and precision not formerly possible with discrete components.

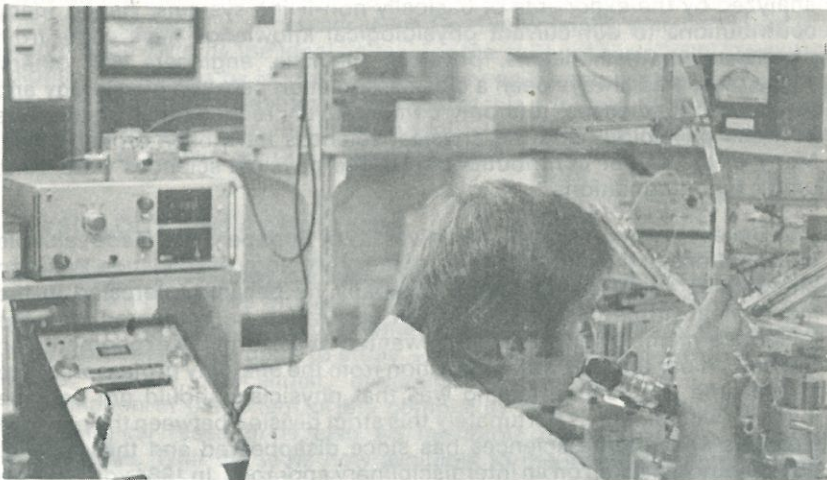


Figure 1. A post-graduate student in physiology doing precise electrical measurements in isolated renal tubules.

I should like to illustrate, by results from my own research, some of the advantages of studying a physiological problem by using the principles and developments from other sciences: We are investigating the mechanisms of active sodium transport across epithelial cells. This is a fundamental process in living systems and is, amongst others, responsible for the functioning of our nervous system and kidneys. For our investigation we make use of very basic principles in physics and electrical engineering to analyze data. Not only does this approach make new tools available for our studies, but it also presents us with new ways of expressing ourselves, i.e., in the precise and logical ways of mathematical and electrical models.

The following diagram illustrates very simply the philosophical idea underlying ion transport mechanisms:



Forces may be passive, active or coupled.

The mass, or ion transported, is usually known while the flux can be readily measured. The interesting problem is the force that moves the ion and this is the main object of our investigations. It is commonly accepted that the active transport of ions across epithelia occurs by virtue of ion-specific pumps. Most of the studies on these pumps are done by chemical analysis and pharmacological experiments. However, very little is known about the mechanisms of these pumps since most of the earlier studies have concentrated on a kinetic definition of the pumps by measuring rates of transport of the ions under various conditions.

Advances in electronics have made it possible to design a system whereby very accurate measurements of intracellular potentials are possible, using a microelectrode and our results can be interpreted very precisely by means of an electrical model. When the transporting cells were penetrated with a microelectrode, stable negative potentials averaging about 100mV were recorded. This observation was not in accordance with earlier results, which had reported positive potentials. In the light of this and other results an electrical model representing the mechanism of the active Na transport pathway could be constructed.

Very simply the active pathway can be represented by an equivalent model as shown in figure 2. However, in view of the following two important findings a more realistic representation of the pathway can be presented.

- (1) When a microelectrode is introduced into the cell there is a substantial resistance, accounting for approximately 75% of the total resistance, between the microelectrode and the outer solution.

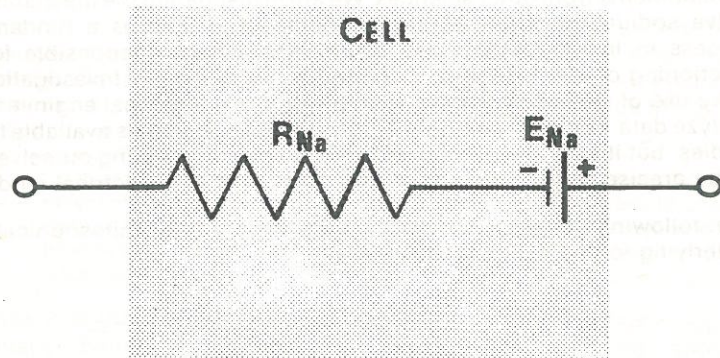


Figure 2. A simplified model representing the active sodium transport pathway. The driving force (emf) of the transepithelial current is the  $E_{Na}$ , and resistance to flow is the  $R_{Na}$ .

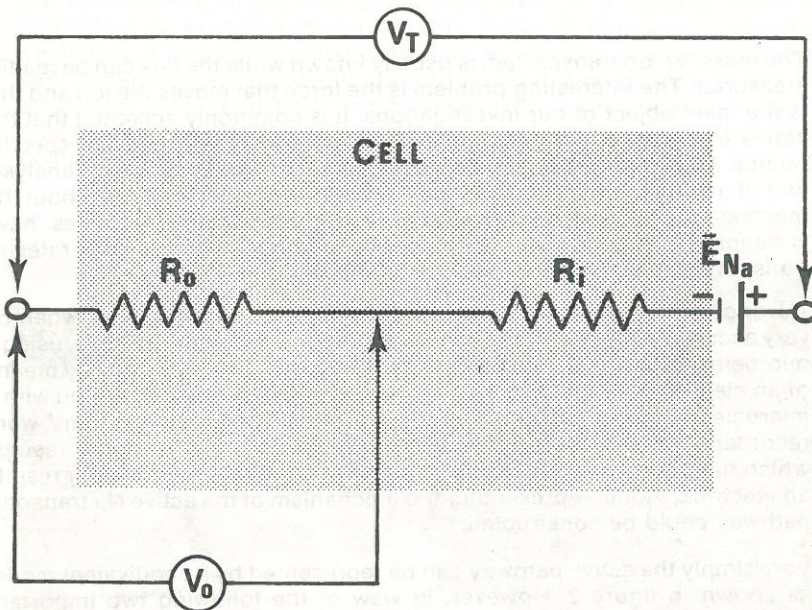


Figure 3. Electrical equivalent circuit of the active sodium transport pathway. The inner barrier is modelled with a Thévenin equivalent consisting of emf,  $E_{Na}$ , and resistance,  $R_i$ .  $V_o$  is the voltage across the outer barrier, measured with a microelectrode, and  $R_o$  is the resistance of the outer barrier.

- (2) Other evidence<sup>8</sup> indicates that the locus of the "pump" is on the inner cell membrane. Therefore, the sodium pathway may be modelled by an equivalent circuit as in figure 3 and our results can be interpreted by means of this model.

The various parameters of the model can be determined experimentally and used in the interpretation of results. For example, in one of our experiments we investigated the mechanisms whereby anti-diuretic hormone (ADH) stimulates active sodium transport across frog skin and other epithelia. From our results we could conclude that ADH has no noticeable effect on the sodium pump, but increase sodium transport by decreasing the resistance to sodium entry at the outer barrier by 56% of control values.

I hope that by these examples I have succeeded in demonstrating some of the advantages presented to the physiologist by using an interdisciplinary approach to study a particular problem.

The majority of examples used illustrates the interrelationship and interdependence of physiological study and the physical sciences. This was done because the barrier between physiology and the physical sciences is often difficult to overcome, probably due to a reluctance by biologists to make use of mathematics and physical principles. In fact, in physiological study many disciplines are involved, whether pharmacology, zoology, veterinary sciences, pathology or engineering.

While the interdisciplinary approach to physiological study has numerous advantages, as evident from the vast expansion of our knowledge, it has also placed additional demands on the scientist and student. The most obvious one is that the problems now confronting the scientist require techniques and basic knowledge of many other disciplines, such as physics, engineering, chemistry and mathematics. Unfortunately each discipline has its own techniques, formalism, and even its own "language". It is therefore imperative that the scientist should learn the new language to enable him to participate fully, and to communicate with other scientists in the field. Communication is a real problem — for the physiologist as well as for the physical scientist. According to Stanford, the physical scientist or engineer will neither comprehend the problems of the life scientist nor will he contribute to their solution until he can communicate effectively with the life scientist.<sup>9</sup> I would like to add that communication is essential to obtain any kind of cross-fertilization of ideas between the various disciplines.

The student in life sciences is also affected by these developments. We see that, to understand physiological principles, he must now have at his command a multitude of concepts from the pure sciences, especially physics, chemistry and mathematics (particularly calculus). However, after the first year of study the students in biological or medical sciences, regrettably, usually do not receive any additional training in this. It is often left to the teacher in biological sciences to reinforce these concepts during the curriculum. Arguably this is not too great a loss when graduates go to medical, nursing or similar schools and eventually join their respective

professions. It is, however, when the graduate wishes to pursue basic research in the life sciences when his deficiency, in the physical disciplines especially, usually becomes apparent.

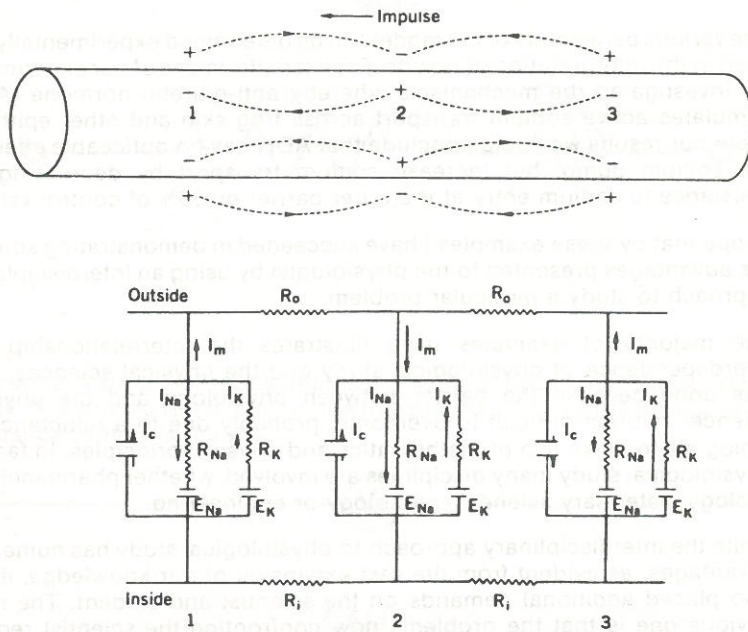


Figure 4. An example of the application of principles from the physical sciences in physiology. From a recent lecture on: The nerve impulse.

Ideally a post-graduate programme should prepare students to function effectively in a working situation. Thus the student should be endowed with the cognitive and problem-solving skills to deal flexibly with changing situations. Unfortunately this is not always the situation with post-graduate students at our universities. Very often we find that the only skills the student learns are those involved with his own particular research project. The danger of this is that the student becomes very restricted in his field of research, and so specialized and devoted to a specific problem that he is only qualified to continue research in that particular area. Worse still, that research can often be conducted in a particular department only. This is not a good way of training a student for a working situation. In principle I agree with the views of Prof. A.C. Burton<sup>1</sup> which states that training to the doctorate level should be regarded as preparing a student to tackle any problem in his chosen field.

It is not easy to select the proper training schedule for post-graduate students. Since we want to produce a more flexible student, we expect our own post-graduate students to take certain related courses in addition to their research topics. Since post-graduate students in physiology usually engage in basic biological or medical research, the problem confronting them could also require techniques and concepts from other disciplines. We, therefore, reinforce concepts from disciplines like biochemistry, physics, pharmacology and mathematics, where applicable to their physiological study, during their post-graduate studies. Instrumentation is vital to the life scientist engaged in research. Often the answer to a particular problem is technical, requiring a particular knowledge. For this reason we provide short courses in biophysics and bioelectronics to our post-graduate students. Biophysics is the application of techniques and approaches of the physical sciences to the problems of the life sciences, while bioelectronics teaches the principles and application of electronic instrumentation. I am of the opinion that with this kind of background our post-graduate students are more flexible and better prepared to continue their research in a working situation outside the university.

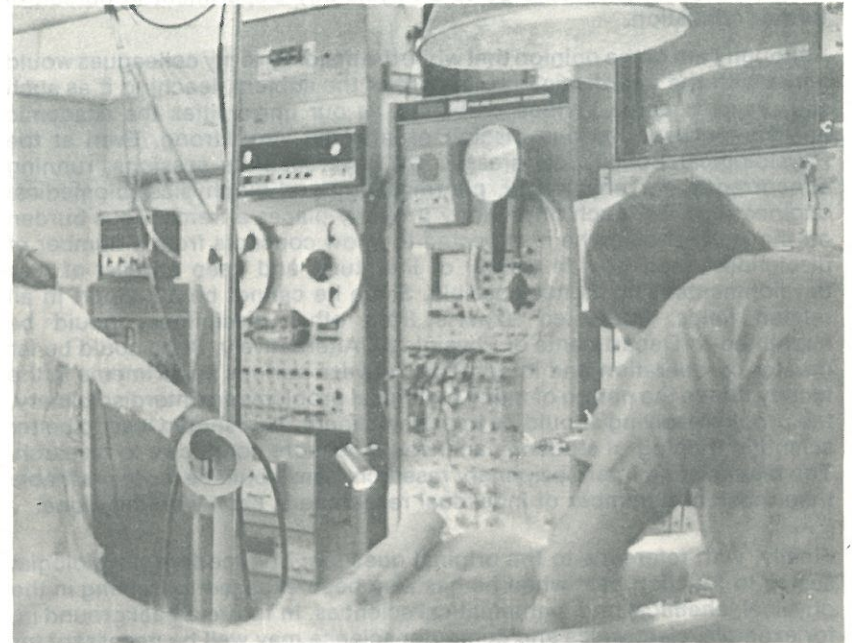


Figure 5. In a modern physiology laboratory instrumentation is of vital importance.

Because of the modern interdisciplinary approach to physiology, researchers from many other disciplines are actively involved in analyzing its fundamental problems. Hence, the strict academic barriers that exist between various disciplines no longer seems valid. I have noticed that at a number of American universities physiology is taught by an interdisciplinary approach. In 1978 the Department of Physiology at the University of Illinois had more than 90 post-graduate students. These included graduates from medical schools and from zoology, biology, mathematics and other departments. Certain lectures in physiology were also given by experts from other departments, as those of botany, veterinary sciences (endocrinology) and agriculture (genetics). Despite the diverse backgrounds of the students and professors they had a common interest, namely, studying the fundamental principles of living systems, which is by definition the field of physiology.

The situation described above is close to the ideal one, and certainly conducive for research. It is difficult to duplicate the situation at our own universities. Firstly we do not have the large student number or staff of the American Departments. Also, our students in the Science Faculty are mainly department-orientated and not problem-orientated when in search of research topics. Hence, it is relatively rare that a student majoring in another department would go to a Physiology Department in pursuit of further education.

Although I am of the opinion that while the majority of my colleagues would agree with the interdisciplinary nature of the subject, teaching it as such still presents some serious problems. At our universities the academic barriers between various disciplines are still very strong. Even at the Physiological Society congresses we have separate sessions, running concurrently, for physiology, pharmacology and biophysics (biomedical engineering). To teach physiology properly places a tremendous burden on the lecturer since he is expected to know concepts from a number of disciplines, read a wide variety of literature, and keep abreast of new developments. This is not possible. Since he cannot be an expert in all related fields, interested experts from other disciplines should be appointed to Departments of Physiology. Alternatively, there could be far greater co-operation and integration between various departments in the faculty. Since the nature of many biological problems are interdisciplinary, the problem-solving should be interdisciplinary. This should lead to better scientific training of students, and would be more conducive to research. The results of an interdisciplinary research team would be more profitable than those of a number of individual researchers, each working alone.

Finally, with reference to the original question: The modern physiologist seems to function best when he has also been exposed to training in the physical, chemical and mathematical sciences. In future a background in, for example, electronics and computer science may well be necessary for the "complete" physiologist. Academic compartmentalization in pure physiological research is definitely disappearing. Strangely enough the era of the traditional butchers, bakers, and candlestickmakers has gone too: as things stand today, they are all physiologists, of "one type or another."

## ACKNOWLEDGEMENTS

Mr. Vice-Chancellor, I have just expressed my views on the modern trends in Physiology as well as my approach to the teaching and research of the subject. I also feel obliged, on this occasion, to acknowledge gratefully the considerable influence the following persons have had on my training as a scientist as well as instilling in me a proper philosophy of research: Dr. D. van Zyl Engelbrecht of the Department of Zoology at Stellenbosch University; Prof. A.G. Everson Pearse of the Royal Post-graduate Medical School at the University of London; Prof. Sandy I. Helman of the Department of Physiology and Biophysics at the University of Illinois.

\* \* \*

Mr. Vice-Chancellor, it is an honour to be the first person appointed to the Chair of Physiology at the University of the North. It is, therefore, my privilege to accept this appointment with due appreciation of the responsibility.



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