

Nutrition: A Reservoir for Integrative Science

S. H. Zeisel,¹ L. H. Allen, S. P. Coburn, J. W. Erdman, M. L. Failla, H. C. Freake, J. C. King and J. Storch

Long Range Planning Committee, American Society for Nutritional Sciences

ABSTRACT In the last twenty years, powerful new molecular techniques were introduced that made it possible to advance knowledge in human biology using a reductionist approach. Now, the need for scientists to deal with complexity should drive a movement toward an integrationist approach to science. We propose that nutritional science is one of the best reservoirs for this approach. The American Society for Nutritional Sciences can play an important role by developing and delivering a cogent message that convinces the scientific establishment that nutrition fills this valuable niche. The society must develop a comprehensive strategy to develop our image as the reservoir for life sciences integration. Our efforts can start with our national meeting and publications, with the research initiatives for which we advocate, with our graduate training programs and with the public relations image we project for ourselves. Defining the image and future directions of nutrition as the discipline that can integrate scientific knowledge from the cell and molecule to the whole body and beyond to populations can be the most important task that our society undertakes. If we do not effectively meet this challenge, a golden opportunity will pass to others and nutritional scientists will be left to follow them. *J. Nutr.* 131: 1319–1321, 2001.

KEY WORDS: • *nutrition* • *American Society for Nutritional Sciences* • *long range planning* • *scientific integration*

Defining the image of nutrition

It is likely that the skills of nutrition scientists will become increasingly valuable as it becomes more necessary to translate from molecular events to whole body metabolism to behaviors. It is important that we identify the opportunities for nutrition to become a more valued science that occupies an important niche as a cross-disciplinary, integrationist life science. The American Society for Nutritional Sciences (ASNS) can play an important role in focusing our discipline's image so that our research and training programs are viewed as being unique assets within the relevant scientific communities in which we work. Defining the image of nutrition may be the most important task that our society undertakes. This initiative will require that we identify those features of nutritional science that will provide us with the greatest opportunities, and then undertake a coordinated effort to develop the relevant innovations in training and research techniques. A sophisticated public relations campaign will be required to promote the unique skills of nutritional scientists.

The ascendance of reductionism in life sciences

During the last twenty years, powerful new molecular techniques have generated incredible insights into human biology using a reductionist approach. By reductionism we refer to the scientific approach aimed at identifying the molecules in-

involved in biological events and examining them in their purified form or in simple systems. Biochemistry (physiology, pharmacology, and other) departments, once based on metabolic and nutritional biochemistry, evolved during the 1980s and 1990s so that they focused almost exclusively on molecular events. This was a heady time for biologists, and most basic life science disciplines converged in the use of a reductionist approach to discover new knowledge. As a result, the reservoir of knowledge about nutritional/metabolic biochemistry, knowledge that used to be at the core of such departments, was allowed to diminish. The interest in and capacity to perform metabolic research in these departments became limited, and the graduates of these doctoral programs now often have little or no exposure to metabolism. This means that most graduates of basic life science departments have strong skills focused on reduction of biology to molecular events, but few of the skills required to integrate these events into multiorgan and whole-body metabolic pathways. Although many nutrition departments also included reductionist approaches to varying degrees in their curricula, for the most part, nutrition students continued to be trained in the broader areas of metabolism and metabolic regulation, and, more recently, epidemiology and behavior. Although they may have lacked some of the depth of the narrowly focused training, they retained the broader perspectives and skills required to collect and link information across the continuum of gene-whole body-clinical-community. Although in some cases broader skills were not fully valued during the ascendance of the reductionist approach, there is now a window of opportunity because there is growing recognition that these skills will

¹ To whom correspondence should be addressed at University of North Carolina at Chapel Hill, CB#7400, McGavran Hall Room 2212, Chapel Hill, NC 27599-7400. E-mail: steven_zeisel@unc.edu.

be essential for the next phase of biological science (Shulman 1998).

Nutrition is an important reservoir of integrationism

As we rapidly approach the time when the entire human genome is sequenced, a pressing need arises for scientific integrationism. There is a strong case to be made that the nutritional sciences are a vital reservoir of these skills. It is critical that the discipline of nutrition, led by the ASNS, develop and deliver a cogent presentation that convinces the scientific establishment that nutrition fills this valuable niche. Today we are faced with difficult questions dealing with the complex interactions that determine phenotype. Basic science disciplines are becoming increasingly aware that an understanding of metabolism and metabolic regulation is central to the understanding of how molecular events result in life itself. How do you explain phenotype once you know genotype? What are the complex effects on metabolism of deleting or changing expression of a gene? How do you design a drug to modulate metabolism? How does behavior modify phenotype? To approach such questions, it is necessary to understand, for example, how nutrition modulates the milieu in which biochemical and genetic mechanisms operate. Gene expression is regulated by interactions with nutrients and other gene products in a tissue-specific manner. In turn, tissue-specific interactions must be modulated by organ-organ interactions. The understanding of homeostatic mechanisms is an example of an integrationist goal.

Although knockout gene methodology has taught us a great deal about the functions of some genes, it is certain that complex homeostatic responses to gene deletions modulate the phenotype we observe in such animals. Clinicians, often forced to use an empirical approach for identifying appropriate therapies for disease, require that basic scientists combine multiple molecular events, gene responses, metabolic responses and behavioral responses so as to present an integrated picture of disease processes.

Integration of molecules to metabolism is only the first stage in the process; eventually we also must integrate metabolism and behaviors. Epidemiologic approaches have provided intriguing and sometimes conflicting information about the role of nutrients in disease processes. Nutritional science is particularly well placed to take these observations and support them with mechanistic understanding. The need for scientists to deal with complexity should drive a movement toward an integrationist approach to science. We have a long-established presence in this area; thus, we are uniquely well positioned to take the lead in the integrationist movement. However, we must move aggressively; many other disciplines are beginning to recognize the same opportunities. Our society can help to establish nutrition's niche as a lead discipline that brings together our fellow scientific disciplines in the pursuit of integration; if we do not act swiftly, a golden opportunity will pass to others and nutritional science will be left to follow them.

How does ASNS proceed?

We do not believe that the mere repackaging of what we do will suffice to place nutrition appropriately. Thoughtful planning, educational programs and new methodology will be required. The society must develop a comprehensive strategy to develop our image as a reservoir of knowledge and leader for the integration of life sciences. Our efforts can start with our national meeting and publications, with the research initia-

tives for which we advocate, with our training programs and with the public relations image we project for ourselves.

Our national meeting and publications

A well-designed and coordinated series of plenary sessions and workshops should be aggregated during our national meeting under the overarching theme of nutrition as an integrationist discipline. Respected speakers should highlight problems in modern biology solved by integrative nutrition approaches used by nutritional scientists who use cutting-edge methodology to not only permit reduction to the smallest event, but also to integrate these events into metabolic pathways and beyond. Presentations on the use of elegant methods (e.g., microarrays, metabolic modeling, knockouts, nuclear magnetic resonance spectroscopy, accelerator mass spectrometry, positron emission scanning, epidemiological techniques and behavioral approaches), perhaps with special modification so that they address the integration process, should acquaint our members with the latest methodology. Such sessions also will serve to convince our colleagues in other disciplines that nutrition scientists are leaders in using the integration approach. The mathematical modeling of metabolism (e.g., metabolic control analysis, which allows control to be distributed among multiple enzymes rather than one rate-limiting step) (Fell 1997), the integration of the identification of vitamin A deficiency-induced blindness with vitamin A metabolism, the genetic modification of oil seeds to make them overproduce this vitamin, and the community interventions that deliver this to populations in a culturally acceptable manner can be presented as examples of integrative research that crosses disciplines. We could present the integration of our understanding of the molecular signals that control appetite and energy expenditure with the metabolic phenomena underlying lipogenesis and with the behavioral modulators of eating, ending with the development of a range of therapies for obese individuals. The use of genetic markers to identify susceptible populations in nutrition epidemiology or in human clinical nutrition should be presented under this umbrella concept. The total meeting package should be designed so that colleagues from other disciplines at Experimental Biology will attend our sessions to learn how we integrate. Coordination of these sessions is necessary and will require careful attention to the central message that we hope to transmit.

Our journal should regularly publish an issue that includes papers (perhaps from the annual meeting sessions) that reinforce this integrationist image. This special issue should be widely disseminated to other disciplines. Perhaps key articles can be placed in the *FASEB Journal* to further reinforce this image.

Funding initiatives

Our society and its members are actively involved in advocating funding from the National Institutes of Health and the U.S. Department of Agriculture. ASNS must sell the concept that the integration of molecular, metabolic and behavioral events using a nutrition perspective is the next hot area once the genome has been sequenced. We must make it clear that the complexity of our grant proposals is a virtue and not a weakness. We want to encourage requests for coordinated efforts to introduce integrationist perspectives into research initiatives, preferably initiatives that use nutrients as examples. Interesting examples to pursue include the following: folate genetics, methyl and homocysteine metabolism, and

heart disease or cancer; or fatty acid metabolism, regulation of gene expression, obesity and progression of diabetes.

Our training programs

There are many excellent training programs in nutrition, but the set of skills and knowledge base of nutrition graduate students is not clearly apparent, particularly to the non-nutrition community. When we consider a biochemist, we have an understanding of how this person has been trained, whereas we have no equivalent insight when we speak of a nutritional scientist. The ASNS can help resolve this identity crisis by providing clear guidelines for training programs.

One approach taken by nutritional science training programs has been to emulate many of the methods of persons from the disciplines with which we interact (biochemistry, physiology, pathology, pharmacology, epidemiology). These methods have enriched our approach, but they should not be the sole training that we provide to students of nutrition. Although, as indicated earlier, many nutritional scientists use state-of-the-art molecular biology techniques and other reductionist approaches, it is an error to limit the scope of a nutrition department to a single type of investigational approach. For many nutritional scientists, graduate training did not focus in depth on a narrow field, but rather encompassed a much broader area. Our discipline loses something special if the field is defined so that it is acceptable for our students to understand in great depth, for instance, the function of only a

single gene. Nutrition's most valuable niche is based on the ability to integrate as described earlier, and our strategy must be to purposefully design our training programs so that our graduates have this capacity.

Our society must establish a process to identify our strengths in a thoughtful manner, reach some consensus of common elements in a nutrition curriculum and help schools incorporate and teach them. The continuing controversy over optimal nutrient intake for maximum health and longevity indicates the necessity for well-designed integrative studies. Content must be presented in such a way that it becomes clear that nutritional science uses evidence-based approaches that are critical (as well as familiar) to the entrenched health disciplines. Moreover, nutritional science provides an excellent venue for those who seek to build a whole-body perspective from individual molecular events. Concepts such as metabolic control analysis will have a significant influence on the design of integrative metabolic studies, and should be included in nutrition training. Also, we should identify the requirements that employers have for integrationist approaches and make bridges to our students so that nutrition is identified as the place to go to find employment.

LITERATURE CITED

- Fell, D. (1997) *Understanding the Control of Metabolism*. Portland Press, London, UK.
Shulman, R. G. (1998) Hard days in the trenches. *FASEB J.* 12: 255–258.