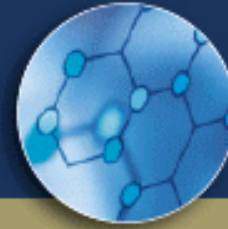




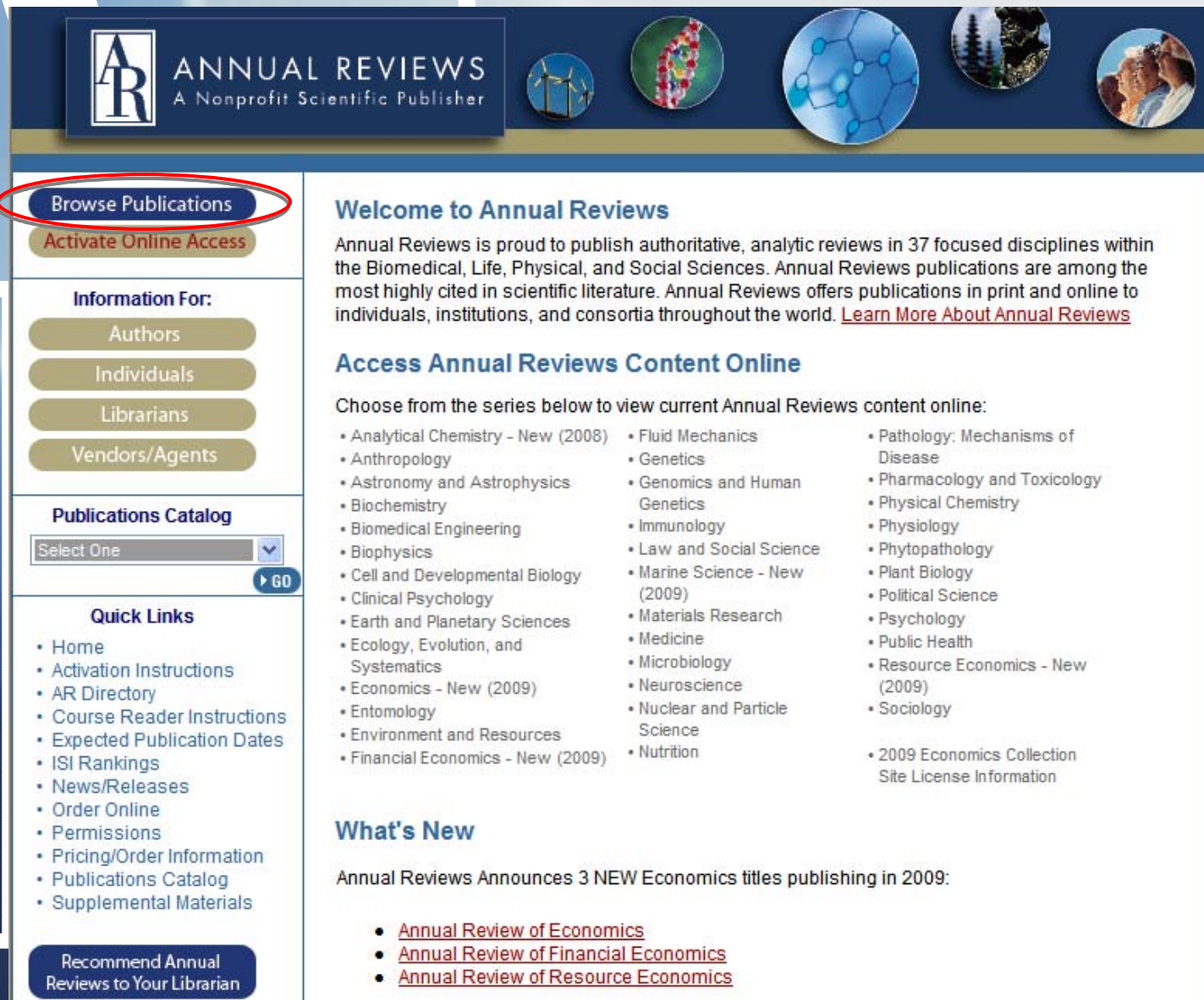
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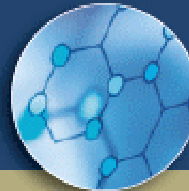
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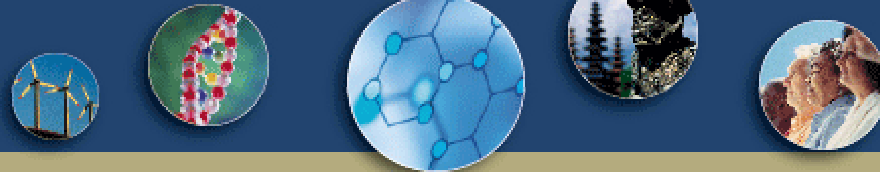
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### ENERGY CONVERTING NADH:Quinone Oxidoreductase (Complex I)

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#### ABSTRACT

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NADH:quinone oxidoreductase (complex I) pumps protons across the inner membrane of mitochondria or the plasma membrane of many bacteria. Human complex I is involved in numerous pathological conditions and degenerative processes. With 14 central and up to 3 accessory subunits, complex I is among the largest membrane-bound protein assemblies. The peripheral arm of the L-shaped molecule contains flavine mononucleotide and eight or nine iron-sulfur clusters as redox prosthetic groups. Seven of the iron-sulfur clusters form a linear electron transfer chain between flavine and quinone. In most organisms, the seven most hydrophobic subunits forming the core of the membrane arm are encoded by the mitochondrial genome. Most central subunits have evolved from subunits of different hydrogenases and bacterial  $\text{Na}^+/\text{H}^+$  antiporters. This evolutionary origin is reflected in three functional modules of complex I. The coupling mechanism of complex I most likely involves semiquinone intermediates that drive proton pumping through redox-linked conformational changes.

#### INTRODUCTION

Section:

As one of the most fundamental metabolic principles, the vast majority of biochemical pathways involves "bound hydrogen" intermediates in the form of NADH, NADPH, or reduced flavoproteins. NADH generated in catabolic pathways is fed into energy converting electron transfer chains via NADH:quinone oxidoreductases. Three enzyme families catalyze this reaction. This review focuses on proton translocating NADH:quinone oxidoreductase. This type of enzyme, usually called complex I, was first described in mitochondria (1), but it is also found in many eubacteria where it is frequently termed NADH dehydrogenase-1 or NDH-1 (2, 3, 4). Moreover, complex I is involved in bacterial photosynthetic electron transport (5, 6). In some

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job, we were spared the worst of that dreadful period.

#### EARLY YEARS IN BALTIMORE

My early years were uneventful. I was a good, but not outstanding, student. During my last two years of high school, to help support the family, I worked part-time in a large meat market as a butcher's assistant. I became quite a skillful meat cutter and was promised a full-time job after high school graduation, a not inconsequential prospect because the United States was still mired in the Depression, and the possibility of college after high school graduation was very remote. All of this changed with the attack on Pearl Harbor by the Japanese on Sunday, December 7, 1941. I can still recall the radio announcer breaking in on the broadcast of the New York Philharmonic Symphony to report that Pearl Harbor had been attacked. The following day, the entire student body of my high school assembled to hear the radio broadcast of President Franklin D. Roosevelt's speech, "December 7, 1941 a date that will live in infamy." I remem-

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**Figure 1** Subcomplexes and subunits of bovine heart complex I. The assignment of subunits to the subcomplexes of complex I was made according to References 18 and 19, and for the central hydrophobic subunits, the figure includes suggestions from Reference 111. Flavoprotein (FP) is part of I $\lambda$  (light yellow), and I $\alpha$  essentially is a combination of I $\lambda$  and I $\gamma$  (yellow). I $\beta$  (blue gray) forms the major part of the membrane integral arm of complex I. Central subunits are in blue, accessory subunits found in all eukaryotic complexes are in red, and metazoa specific subunits are in purple. Subunits marked with an asterisk are predicted to contain a single transmembrane domain (19).

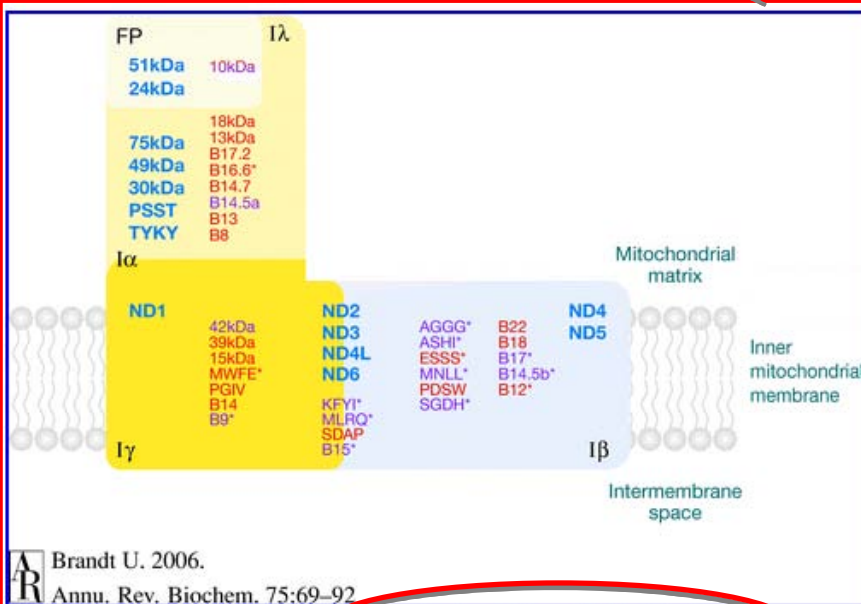
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## Central Subunits

Sequence analysis immediately reveal subunits are highly total of 52–59 transmembrane domains consistently predicted redox prosthetic groups mitochondria and the complex, which part containing the observed for complex I.



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Brandt U. 2006.

Annu. Rev. Biochem. 75:69–92

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Except for some plants, algae, and protists, the seven hydrophobic subunits are encoded by the mitochondrial genome in most eukaryotes (Table 1). However, in some cryptophytic algae such as *Rhodomonas salina* up to 12 subunits are encoded by mitochondria (33). In other organisms

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**Analysis of the Subunit Composition of Complex I from Bovine Heart Mitochondria<sup>\*,S</sup>**

Joe Carroll, Ian M. Fearnley, Richard J. Shannon, Judy Hirst and John E. Walker<sup>†</sup>

From the Medical Research Council Dunn Human Nutrition Unit, The Wellcome Trust/MRC Building, Hills Road, Cambridge CB2 2XY, United Kingdom

Complex I purified from bovine heart mitochondria is a multisubunit membrane-bound assembly. In the past, seven of its subunits were shown to be products of the mitochondrial genome, and 35 nuclear encoded subunits were identified. The complex is L-shaped with one arm in the plane of the membrane and the other lying orthogonal to it in the mitochondrial matrix. With mildly chaotropic detergents, the intact complex has been resolved into various subcomplexes. Subcomplex IA represents the extrinsic arm, subcomplex Ia consists of subcomplex IA plus part of the membrane arm, and subcomplex IB is another substantial part of the membrane arm. The intact complex and these three subcomplexes have been subjected to extensive reanalysis. Their subunits have been separated by three independent methods (one-dimensional SDS-PAGE, two-dimensional isoelectric focusing/SDS-PAGE, and reverse phase high pressure liquid chromatography (HPLC)) and analyzed by tryptic peptide mass fingerprinting and tandem mass spectrometry. The masses of many of the intact subunits have also been measured by electrospray ionization mass spectrometry and have provided valuable information about post-translational modifications. The presence of the known 35 nuclear encoded subunits in complex I has been confirmed, and four additional nuclear encoded subunits have been detected. Subunits B16.6, B14.7, and ESSS were discovered in the SDS-PAGE analysis of subcomplex IA, in the two-dimensional gel analysis of the intact complex, and in the HPLC analysis of subcomplex IB, respectively. Despite many attempts, no sequence information has been obtained yet on a fourth new subunit (mass 10,566 ± 2 Da) also detected in the HPLC analysis of subcomplex IB. It is unlikely that any more subunits of the bovine complex remain undiscovered. Therefore, the intact enzyme is a complex of 46 subunits, and, assuming there is one copy of each subunit in the complex, its mass is 980 kDa.

<sup>†</sup>To whom correspondence should be addressed: Medical Research Council Dunn Human Nutrition Unit, The Wellcome Trust/MRC Bldg., Hills Rd., Cambridge CB2 2XY, UK. Tel: 44-1223-252701; Fax: 44-1223-252705; E-mail: walker@mrc-dunn.cam.ac.uk

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**Abstract:** Complex I purified from bovine heart mitochondria is a multisubunit membrane-bound assembly. In the past, seven of its subunits were shown to be products of the mitochondrial genome, and 35 nuclear encoded subunits were identified. The complex is L-shaped with one arm in the plane of the membrane and the other lying orthogonal to it in the mitochondrial matrix. With mildly chaotropic detergents, the intact complex has been resolved into various subcomplexes. Subcomplex Ilambda represents the extrinsic arm, subcomplex Ialpha consists of subcomplex Ilambda plus part of the membrane arm, and subcomplex Ibeta is another substantial part of the membrane arm. The intact complex and these three subcomplexes have been subjected to extensive reanalysis. Their subunits have been separated by three independent methods (one-dimensional SDS-PAGE, two-dimensional isoelectric focusing/SDS-PAGE, and reverse phase high pressure liquid chromatography (HPLC)) and analyzed by tryptic peptide mass fingerprinting and tandem mass spectrometry. The masses of many of the intact subunits have also been measured by electrospray ionization mass spectrometry and have provided valuable information about post-translational modifications. The presence of the known 35 nuclear encoded subunits in complex I has been confirmed, and four additional nuclear encoded subunits have been detected. Subunits B16.6, B14.7, and ESSS were discovered in the SDS-PAGE analysis of subcomplex Ilambda, in the two-dimensional gel analysis of the intact complex, and in the HPLC analysis of subcomplex I, respectively. Despite many attempts, no sequence information has been obtained yet on a fourth new subunit (mass 10,566 +/- 2 Da) also detected in the HPLC analysis of subcomplex Ibeta. It is unlikely that any more subunits of the bovine complex remain undiscovered. Therefore, the intact enzyme is a complex of 46 subunits, and, assuming there is one copy of each subunit in the complex, its mass is 980 kDa.

**Addresses:** Walker JE (reprint author), MRC, Dunn Human Nutr Unit, Hills Rd, Wellcome Trust MRC Bldg, Cambridge, CB2 2XY England  
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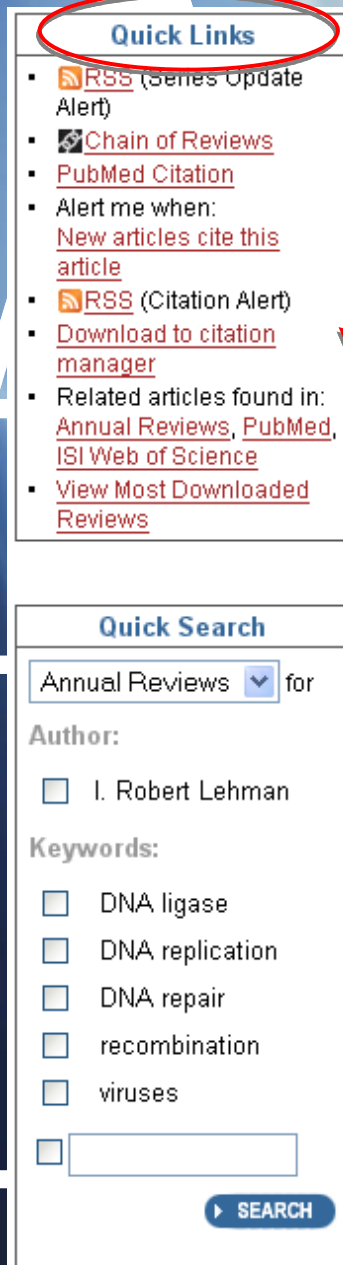
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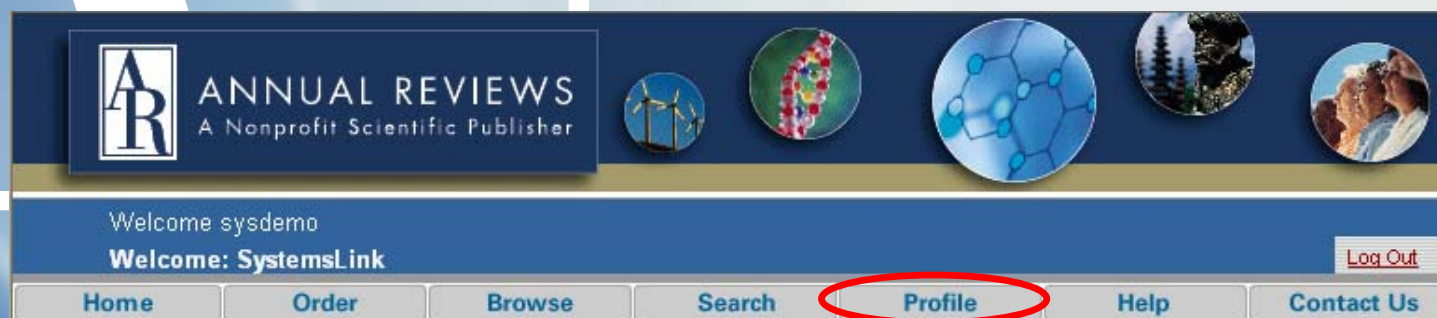
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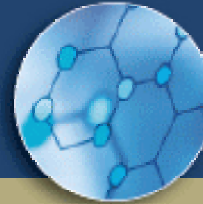
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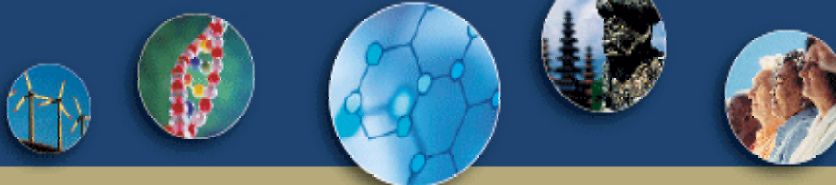
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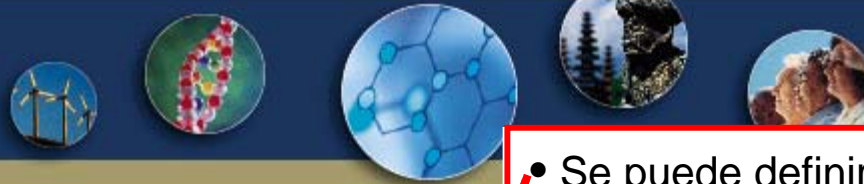
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Johnathan A. Napier

The ability to genetically engineer plants has facilitated the generation of oilseeds synthesizing non-native fatty acids. Two particular classes of fatty acids are considered in this review. First, so-called industrial fatty acids, which usually contain f...

Annual Review of Plant Biology. Volume 58, Page 295-319, Jun 2007

### ✓ **Hydrogenases and Hydrogen Photoproduction in Oxygenic Photosynthetic Organisms\***

Maria L. Ghirardi, Matthew C. Posewitz, Pin-Ching Maness, Alexandra Dubini, Jianping Yu, Michael Seibert

The photobiological production of H<sub>2</sub> gas, using water as the only electron donor, is a property of two types of photosynthetic microorganisms: green algae and cyanobacteria. In these organisms, photosynthetic water splitting is functionally linked to H<sub>2</sub> pr...

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Abstract

## Annual Review of Plant Biology

Vol. 58: 71-91 (Volume publication date June 2007)

(doi:10.1146/annurev.arplant.58.032806.103848)

First published online as a Review in Advance on December 6, 2006

### Hydrogenases and Hydrogen Photoproduction in Oxygenic Photosynthetic Organisms\*

Maria L. Ghirardi,<sup>1</sup> Matthew C. Posewitz,<sup>2</sup> Pin-Ching Maness,<sup>1</sup> Alexandra Dubini,<sup>1</sup> Jianping Yu,<sup>1</sup> and Michael Seibert<sup>1</sup>

<sup>1</sup>National Renewable Energy Laboratory, Golden, Colorado 80401; email: [maria\\_ghirardi@nrel.gov](mailto:maria_ghirardi@nrel.gov), [pinching\\_maness@nrel.gov](mailto:pinching_maness@nrel.gov), [alexandra\\_dubini@nrel.gov](mailto:alexandra_dubini@nrel.gov), [jianping\\_yu@nrel.gov](mailto:jianping_yu@nrel.gov), [mike\\_seibert@nrel.gov](mailto:mike_seibert@nrel.gov)

<sup>2</sup>Colorado School of Mines, Environmental Science and Engineering Division, Golden, Colorado 80401; email: [matthew\\_posewitz@nrel.gov](mailto:matthew_posewitz@nrel.gov)

The photobiological production of H<sub>2</sub> gas, using water as the only electron donor, is a property of two types of photosynthetic microorganisms: green algae and cyanobacteria. In these organisms, photosynthetic water splitting is functionally linked to H<sub>2</sub> production by the activity of hydrogenase enzymes. Interestingly, each of these organisms contains only one of two major types of hydrogenases, [FeFe] or [NiFe] enzymes, which are phylogenetically distinct but perform the same catalytic reaction, suggesting convergent evolution. This idea is supported by the observation that each of the two classes of hydrogenases has a different metallo-cluster, is encoded by entirely different sets of genes (apparently under the control of different promoter elements), and exhibits different maturation pathways. The genetics, biosynthesis, structure, function, and O<sub>2</sub> sensitivity of these enzymes have been the focus of extensive research in recent years. Some of this effort is clearly driven by the potential for using these enzymes in future biological or biohybrid systems to produce renewable fuel or in fuel cell applications.

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## ✓ LEPTIN

Rexford S. Ahima, Jeffrey S. Flier

The discovery of the adipose-derived hormone leptin has generated enormous interest in the interaction between peripheral signals and brain targets involved in the regulation of feeding and energy balance. Plasma leptin levels correlate with fat stores an...

Annual Review of Physiology. Volume 62, Page 413-437, Mar 2000

## ✓ EFFECTS OF NEUROPEPTIDES AND LEPTIN ON NUTRIENT PARTITIONING:

### Dysregulations in Obesity

Bernard Jeanrenaud, Françoise Rohner-Jeanrenaud

Body weight homeostasis is maintained via a series of complex interactions that occur between the brain (particularly the hypothalamus) and the periphery, notably via the hormone leptin, which is synthesized in and secreted from adipose tissue. Under norm...

Annual Review of Medicine. Volume 52, Page 339-351, Feb 2001

## ✓ COMMON ENDOCRINE CONTROL OF BODY WEIGHT, REPRODUCTION, AND BONE MASS

Shu Takeda, Florent Elefteriou, Gerard Karsenty

Bone mass is maintained constant between puberty and menopause by the balance between osteoblast and osteoclast activity. The existence of a hormonal control of osteoblast activity has been speculated for years by analogy to osteoclast biology. Through th...

Annual Review of Nutrition. Volume 23, Page 403-411, Jul 2003

## ✓ FOOD INTAKE AND THE REGULATION OF BODY WEIGHT

Stephen C. Woods, Michael W. Schwartz, Denis G. Baskin, Randy J. Seeley

This chapter reviews the recent literature on hormonal and neural signals critical to the regulation of individual meals and body fat. Rather than eating in response to acute energy deficits, animals eat when environmental conditions (social and learned f...

Annual Review of Psychology. Volume 51, Page 255-277, Feb 2000

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# Resultado de Búsqueda - Leptina

Abstract

## Annual Review of Psychology

Vol. 51: 255-277 (Volume publication date February 2000)  
(doi:10.1146/annurev.psych.51.1.255)

### FOOD INTAKE AND THE REGULATION OF **BODY WEIGHT**

Stephen C. Woods<sup>1</sup> Michael W. Schwartz<sup>2</sup> Denis G. Baskin<sup>2</sup> and Randy J. Seeley<sup>1</sup>

<sup>1</sup>Department of Psychiatry, University of Cincinnati Medical Center, Cincinnati, Ohio, 45267,  
email: [steve.woods@psychiatry.uc.edu](mailto:steve.woods@psychiatry.uc.edu)

<sup>2</sup>Division of Metabolism, Endocrinology and Nutrition, Department of Medicine, University of Washington, and the Puget Sound Veterans Administration Health Care System, Seattle, Washington, 98195,

This chapter reviews the recent literature on hormonal and neural signals critical to the regulation of individual meals and **body** fat. Rather than eating in response to acute energy deficits, animals eat when environmental conditions (social and learned factors, food availability, opportunity, etc.) are optimal. Hence, eating patterns are idiosyncratic. Energy homeostasis, the long-term matching of food intake to energy expenditure, is accomplished via controls over the size of meals. Individuals who have not eaten sufficient food to maintain their normal **weight** have lower levels of adiposity signals (**leptin** and insulin) in the blood and brain, and one consequence is that meal-generated signals (such as CCK) are less efficacious at reducing meal size. The converse is true if individuals are above their normal **weight**, when they tend to eat smaller meals. The final section reviews how these signals are received and integrated by the CNS, as well as the neural circuits and transmitters involved.

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### **LMC International Food Congress 2006: Nutrigenomics and Health – From Vision to Food**

*Scandinavian Journal of Nutrition* 50(0):3 (2006)

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### **THE COW AS A MODEL TO STUDY FOOD INTAKE REGULATION**

[Michael S. Allen](#), [Barry J. Bradford](#), [Kevin J. Harvatine](#)

*Annual Review of Nutrition* 25:523-547 (2005)

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- Stephen C. Woods
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**Annual Review of Cell and Developmental Biology**  
Vol. 22: 23-52 (Volume publication date November 2006)  
(doi:10.1146/annurev.cellbio.21.020404.145837)  
First published online as a Review in Advance on May 5, 2006

**How Does Voltage Open an Ion Channel?**

Francesco Tombola,<sup>1,4</sup> Medha M. Pathak,<sup>2</sup> and Ehud Y. Isacoff<sup>1,2,3,\*</sup>

<sup>1</sup>Department of Molecular and Cell Biology, University of California, Berkeley, California 94720; email: [tombolaf@berkeley.edu](mailto:tombolaf@berkeley.edu)

<sup>2</sup>Biophysics Graduate Group, University of California, Berkeley, California 94720; email: [medha@socrates.berkeley.edu](mailto:medha@socrates.berkeley.edu)

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