

DEUTENOMICS IS ALIVE

-

WHERE DO WE GO FROM HERE

László G. Boros, M.D.

Professor of Pediatrics (retired)

UCLA School of Medicine, Torrance, CA, USA

Janeiro-na-Madeira Winter Summer School 2025

Lectures and actions for EU consortia TopSpec, ARIADNE and ALLODD

DEUTENOMICS

- **how deuterium is distributed in nature and living organisms**
- **how and why deuterium behaves in nature and living organisms in particular ways**
- **what is deuterium's role in adaptive biology, disease and health (e.g.: oncoisotope)**

DEUTENOMICS



All Journals Physics Magazine

<https://doi.org/10.1103/PhysRev.39.164>

Physical Review Journals Archive

Phys. Rev. **39**, 164 – Published 1 January, 1932

A Hydrogen Isotope of Mass 2

[Harold C. Urey](#), [F. G. Brickwedde](#), and [G. M. Murphy](#).

DEUTENOMICS

The Nobel Prize in Chemistry 1934 was awarded to Harold Clayton Urey "for his discovery of heavy hydrogen"

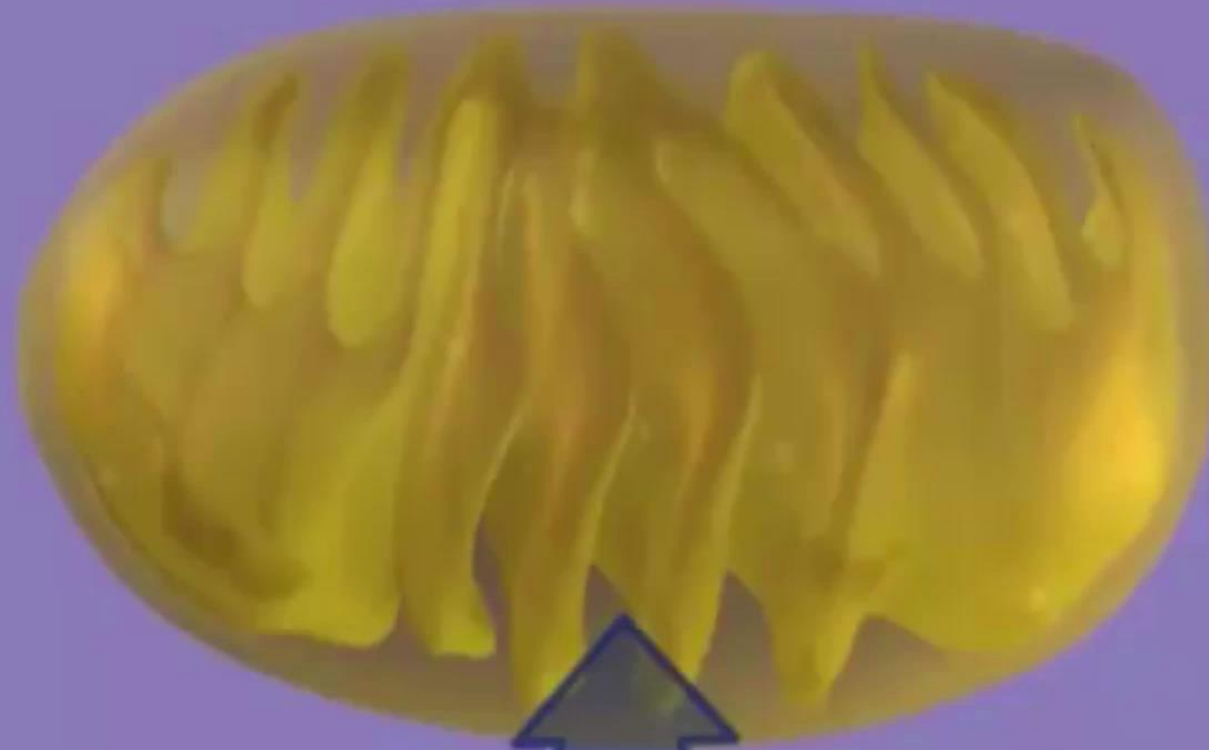
<https://www.nobelprize.org/prizes/chemistry/1934/summary/>



Photo from the Nobel Foundation archive.

Harold Clayton Urey

Prize share: 1/1



Mitochondria

DEUTERIUM FRACTIONATION

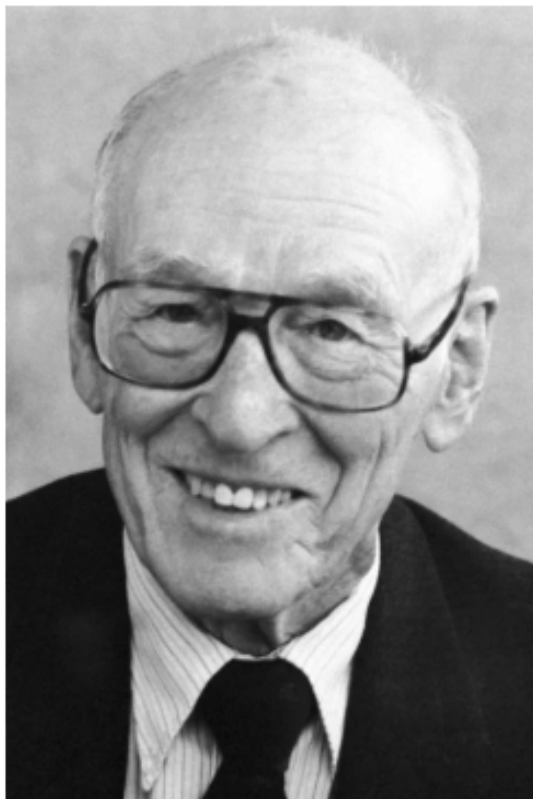


Photo from the Nobel Foundation archive.

Paul D. Boyer

The Nobel Prize in Chemistry 1997

Born: 31 July 1918, Provo, UT, USA

Died: 2 June 2018, Los Angeles, CA, USA

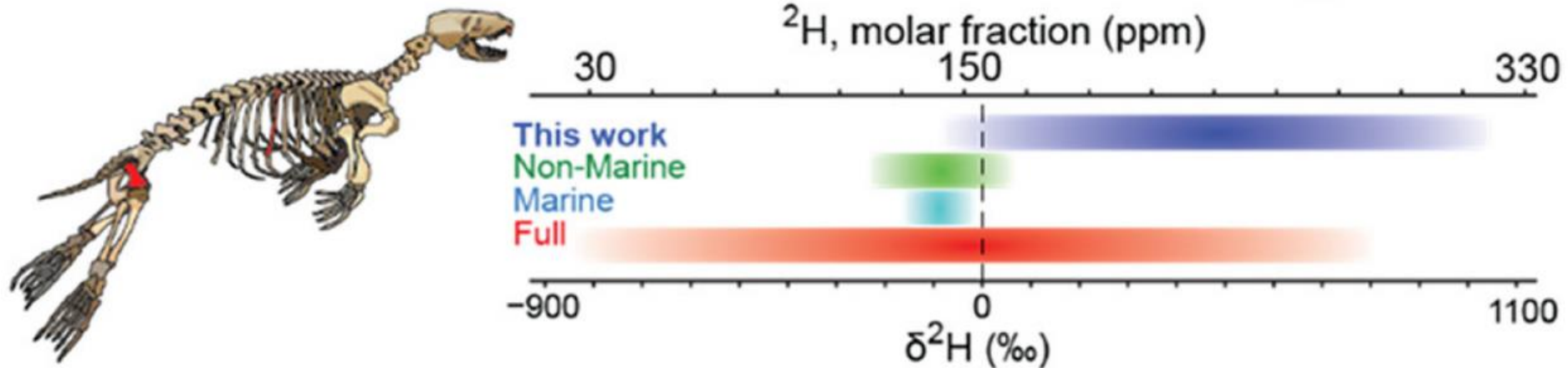
Affiliation at the time of the award: University of California, Los Angeles, CA, USA

Prize motivation: “for their elucidation of the enzymatic mechanism underlying the synthesis of adenosine triphosphate (ATP)”

Prize share: 1/4

<https://www.nobelprize.org/prizes/chemistry/1997/boyer/facts/>

DEUTERIUM AND PHENOTYPE



Abnormal (Hydroxy)proline Deuterium Content Redefines Hydrogen Chemical Mass

Hassan Gharibi,[¶] Alexey L. Chernobrovkin,[¶] Gunilla Eriksson, Amir Ata Saei, Zena Timmons, Andrew C. Kitchener, Daniela C. Kalthoff, Kerstin Lidén, Alexander A. Makarov, and Roman A. Zubarev*

DEUTERIUM AND PHENOTYPE

<https://drive.google.com/file/d/1IG0xI5c52F4wTaOf1hgIGFhUWpS6PvLa/view?usp=sharing>

COMPILATION BY ESZTER ANNA BOROS



<https://doi.org/10.1073/pnas.2310771121>

RESEARCH ARTICLE | ENVIRONMENTAL SCIENCES | 



Large enrichments in fatty acid $^2\text{H}/^1\text{H}$ ratios distinguish respiration from aerobic fermentation in yeast *Saccharomyces cerevisiae*

Ashley E. Maloney  , Sebastian H. Kopf , Zhaoyue Zhang,  +3, and Xinning Zhang   [Authors Info & Affiliations](#)

Edited by Mark Thiemens, University of California San Diego, La Jolla, CA; received June 26, 2023; accepted March 21, 2024

May 6, 2024 | 121 (20) e2310771121 | <https://doi.org/10.1073/pnas.2310771121>

<https://doi.org/10.1073/pnas.2310771121>

Abstract

...

“Our findings point to the broad potential of lipid $^2\text{H}/^1\text{H}$ ratios *as a passive natural tracker* of eukaryotic metabolism with applications to distinguish health and disease, complementing studies that rely on complex isotope-tracer addition methods.”

On 10 Jun 2024, at 19:50, LASZLO G Boros <contact@laszlogboros.com> wrote:

We would like to emphasize the phenotypic role of 2H/1H ratios with adaptive significance, based on many other contributions in the field (please see suggested co-authors).

On 10 Jun 2024, at 19:50, LASZLO G Boros <contact@laszlogboros.com> wrote:

We would like to emphasize the phenotypic role of 2H/1H ratios with adaptive significance, based on many other contributions in the field (please see suggested co-authors).

On Tue, Jun 11, 2024 at 9:48 AM Roman Zubarev <roman.zubarev@ki.se> wrote:

I also think that the PNAs paper in question is a) remarkable, and a potentially crucial point for paradigm changing, and b) disappointing, as it still sticks to the old paradigm that isotopes are spectators rather than active participants, viewing "lipid 2H/1H ratios as a passive natural tracker of eukaryotic metabolism".

It would be great to write a piece promoting the view that heavy isotopes, particularly deuterium, are not merely passive trackers, but are active participants in metabolism, modulating it. If this is the aim of the letter you suggested, am willing to participate.

DEUTENOMICS

<https://doi.org/10.1073/pnas.2412390121>



PNAS

LETTER

MICROBIOLOGY



Active involvement of compartmental, inter- and intramolecular deuterium disequilibrium in adaptive biology

László G. Boros ^{a,2,1}, Stephanie Seneff ^b, Marianna Túri ^c, László Palcsu ^c, and Roman A. Zubarev ^{d,e,f,2}

August 30, 2024 | 121 (37) e2412390121

<https://doi.org/10.1073/pnas.2412390121>

The biosynthetic natural depletion of deuterium (^2H) in palmitic acid of tumor cells, when compared to water of fresh growth medium, readily distinguishes respiration from fermentation, as elegantly reported by Maloney et al. <https://doi.org/10.1073/pnas.2310771121>

<https://doi.org/10.1073/pnas.2412390121>

Accelerated cellular growth remarkably decreased deuterium to protium ($^2\text{H}/^1\text{H}$) ratios, particularly in glycerol-respiring cells, by about 200‰ (~125 ppm).

<https://doi.org/10.1073/pnas.2412390121>

The authors conclude that metabolite $^2\text{H}/^1\text{H}$ ratios may be used “as passive natural trackers of eukaryotic metabolism” that complement complex isotope-tracer methods.

<https://doi.org/10.1073/pnas.2412390121>

The importance of water and product isotope chemistry is evident, which allows a systematic and, more importantly, a mechanistic interpretation, shifting the emphasis from passive to active role of deuterium in the regulation of metabolism in adaptive biology.

<https://doi.org/10.1073/pnas.2412390121>

While fatty acids show a deuterium depleted (“depleted”) profile over extracellular water in rapidly dividing cells, another natural ^2H tracer study showed abnormally high deuterium content in collagen, just to redefine hydrogen chemical mass in biology.

<https://doi.org/10.1073/pnas.2412390121>

Notably, $\delta^2\text{H}$ values in (hydroxy)proline of collagen extracted from grey seals show about twice as much deuterium as its ceiling (~157 ppm) in seawater. This corresponds to at least four times higher $\delta^2\text{H}$ than in any previously reported biogenic sample.

<https://doi.org/10.1021/jacs.1c12512>

<https://doi.org/10.1073/pnas.2412390121>

As diet was ruled out as a plausible mechanism for such anomalous enrichment, evolution seems to depend on deuterium-related regulatory processes via submolecular proton tunneling event (reaction) architectures, with coinciding significant isotope fractionation properties.

<https://doi.org/10.1073/pnas.2412390121>

There are apparent adaptive mechanisms: Some derive from traditional biochemistry, whereas others are yet to be clarified behind the overwhelming disequilibrium patterns in compartmental, inter- and intramolecular deuterium levels reported in recent studies.

[https://doi.org/10.1016/S0306-9877\(98\)90178-5](https://doi.org/10.1016/S0306-9877(98)90178-5)

<https://doi.org/10.1073/pnas.2412390121>

The mechanism of accumulation of deuterons in specific imino acids of bone collagen high above natural mean oceanic water abundance is another example, yet more challenging to answer.

<https://doi.org/10.1021/jacs.1c12512>

<https://doi.org/10.1073/pnas.2412390121>

This phenomenon, seen in predators with phenotypic adaptation to rapid dives in water, likely involves instant, reversible isomerase reactions with selective proton tunneling, nuclear quantum destabilization of metabolic water protons, and thus significant deuterium discriminating properties in hydrophobic cellular and mitochondrial nanoconfinements.

<https://doi.org/10.1021/acs.accounts.8b00226>

<https://doi.org/10.1021/acs.jpcclett.9b01835>

<https://doi.org/10.1073/pnas.2412390121>

We suggest that deutenomics, the study of inherent autonomic hydrogen isotope discrimination processes in nature, should be introduced into translational research. It is important to determine the magnitude of intrinsic kinetic isotope effects, as they are critical in deuterium fractionation, yet often misinterpreted.



<https://doi.org/10.1073/pnas.2412390121>

The Human Deutenome should also not be ignored as an active player (as opposed to passive tracker) in forming the biological reaction coordinate.

<https://doi.org/10.1074/mcp.RA120.002231>



Slight Deuterium Enrichment in Water Acts as an Antioxidant:
Is Deuterium a Cell Growth Regulator?

[Xuepei Zhang](#)¹ · [Jin Wang](#)^{1,2} · [Roman A. Zubarev](#)^{1,3,4}  



NATIONAL DEUTENOMICS INSTITUTE - USA

<https://discourse.nomineesforthepeople.com/t/laszlo-g-boros/73708/14>

349

László G Boros

■ America's Health reviewed, department-of-health-and-hu... department-of-education, department-of-agriculture, 349 votes

Vote

NATIONAL DEUTENOMICS INSTITUTE - USA

<https://discourse.nomineesforthepeople.com/t/laszlo-g-boros/73708/14>

349

László G Boros

■ America's Health reviewed, department-of-health-and-hu... department-of-education, department-of-agriculture, 349 votes

Vote

Agency or agencies for which nominator feels nominee is best suited:

- **Department of Health and Human Services**
- **Department of Education**
- **Department of Agriculture**

NATIONAL DEUTENOMICS INSTITUTE - USA

<https://discourse.nomineesforthepeople.com/t/laszlo-g-boros/73708/14>

349

László G Boros

■ America's Health reviewed, department-of-health-and-hu... department-of-education, department-of-agriculture, 349 votes

Vote

Agency or agencies for which nominator feels nominee is best suited:

- **Department of Health and Human Services**
- **Department of Education**
- **Department of Agriculture**

NATIONAL DEUTENOMICS INSTITUTE - USA

<https://discourse.nomineesforthepeople.com/t/laszlo-g-boros/73708/14>

349

László G Boros

■ America's Health reviewed, department-of-health-and-hu... department-of-education, department-of-agriculture, 349 votes

Vote

I have been proposing a new National Deutenomics Institute (NDI - est. 2025) for a few years now and hopefully this is becoming an urgent reality with the new administration under Bobby's radar!

NATIONAL DEUTENOMICS INSTITUTE - USA

<https://discourse.nomineesforthepeople.com/t/laszlo-g-boros/73708/14>

349

László G Boros

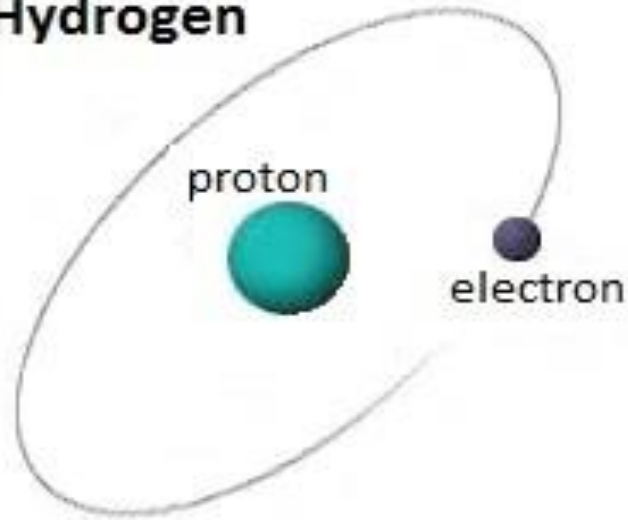
■ America's Health reviewed, department-of-health-and-hu... department-of-education, department-of-agriculture, 349 votes

Vote

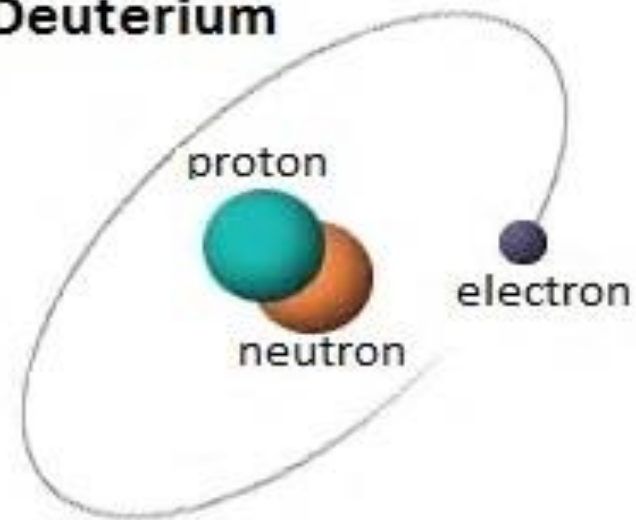
I have been proposing a new National Deutenomics Institute (NDI - est. 2025) for a few years now and hopefully this is becoming an urgent reality with the new administration under Bobby's radar!

NATIONAL DEUTENOMICS INSTITUTE - USA

Hydrogen



Deuterium



THANK YOU!