Oxygen Mediated Ketogenic Nanolubrication of ATP Synthase by Deuterium Depleted Low Viscosity Metabolic Water in Mitochondria

Presentation · May 2016

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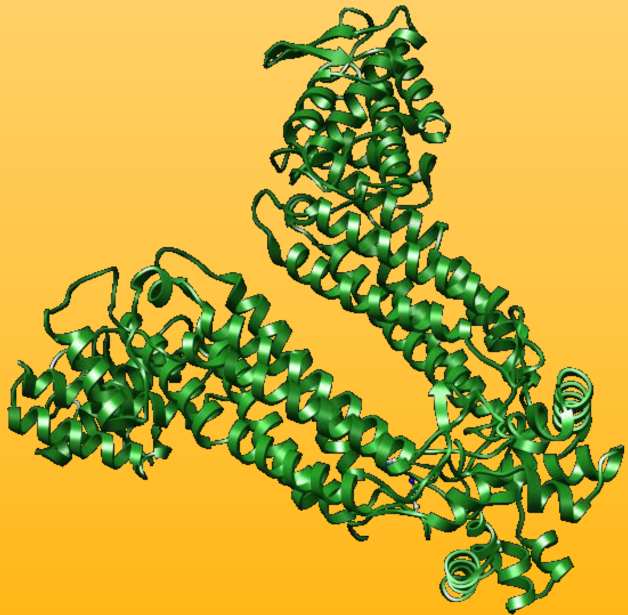

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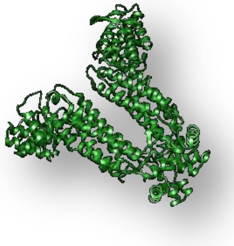
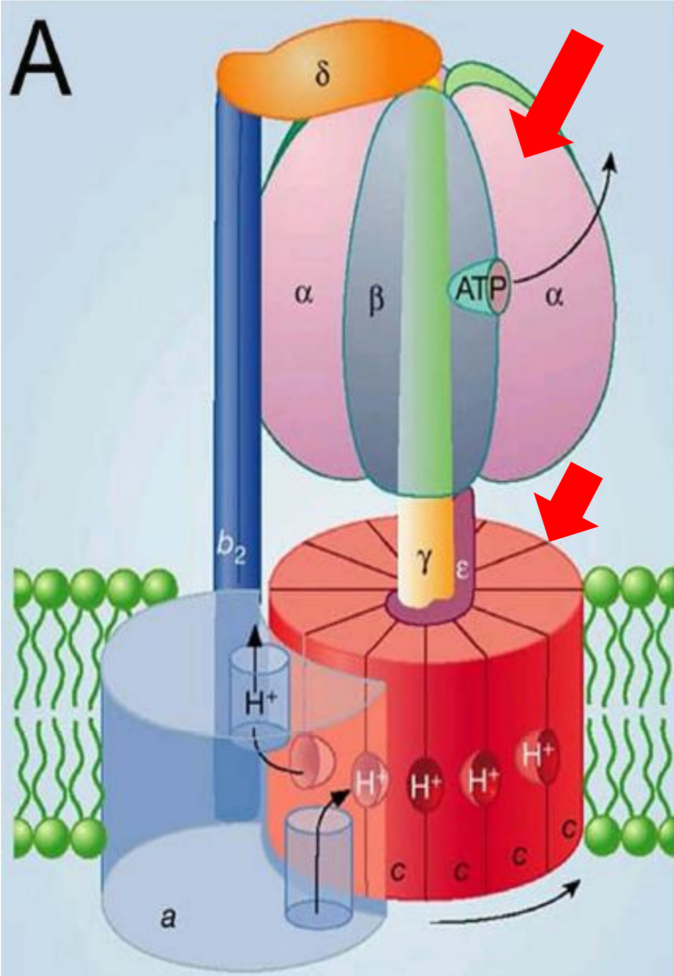
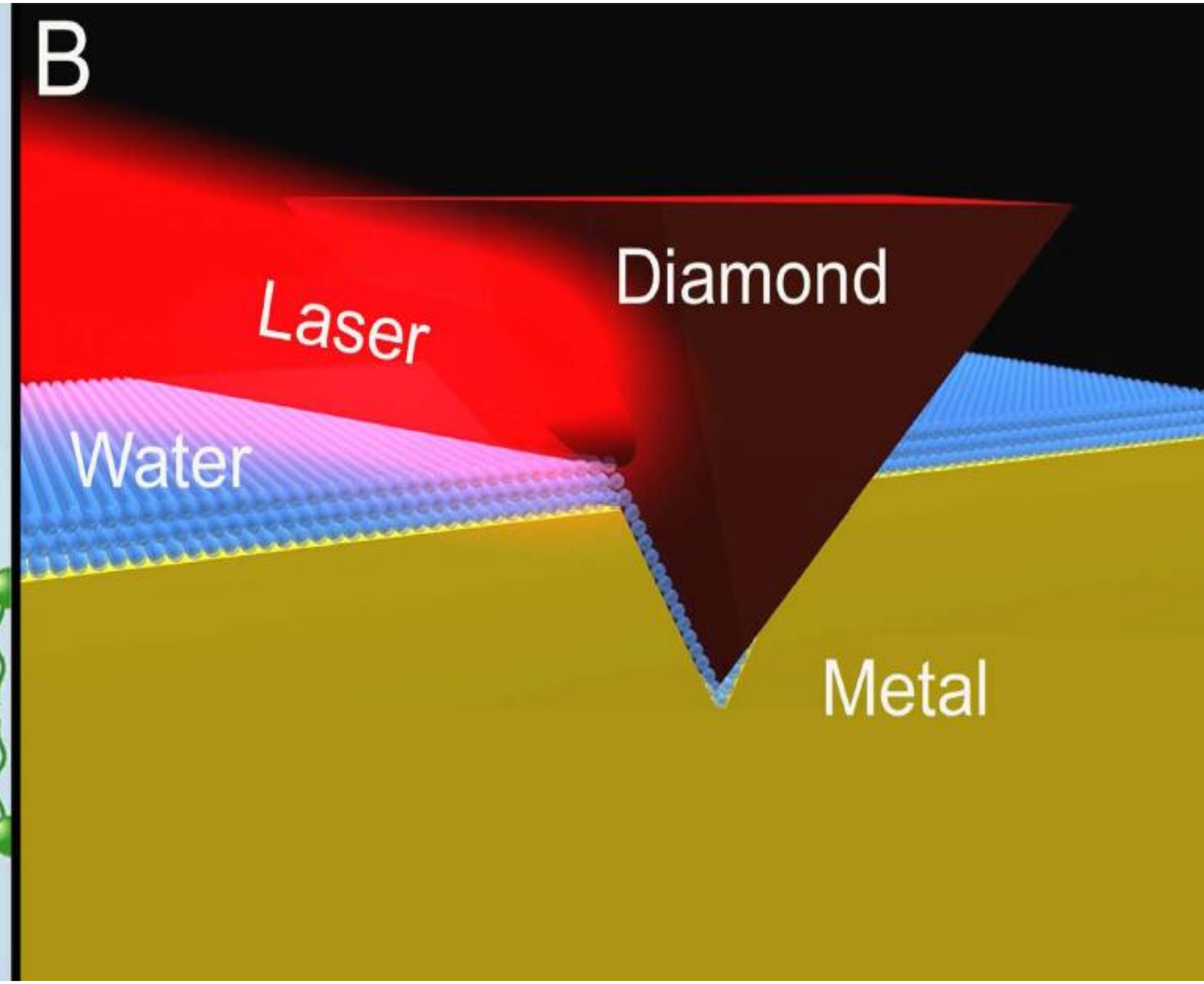


OXYGEN MEDIATED KETOGENIC NANOLUBRICATION OF ATP SYNTHASE BY DEUTERIUM DEPLETED LOW VISCOSITY METABOLIC WATER IN MITOCHONDRIA

University of South Florida
April 29, 2016

László G. Boros, M.D., Adjunct Professor of Pediatrics (Endocrinology & Metabolism), Harbor-UCLA Medical Center, Torrance, California, USA

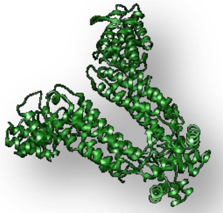




Mitochondrial nanomotor (A): During ATP synthesis, the rotor turns about 9000 times per minute, where the lubricating water's viscosity controls velocity with significant deuterium induced kinetic isotope effects (Dorgan and Schuster 1981 J. Biol. Chem)

Artists view of the principle of light-induced low viscosity single layer interfacial water "flooding" a nanoindentation. Blue spheres are water molecules (H-O-H) forming the nanoscopic single water layer confined in the space between the diamond tip and nanoindentation from the direction of infrared light (B) (Sommer, et al. 2015 Nature Scientific Reports). Reprinted by permission from Macmillan Publishers Ltd: [NATURE] (Cross, 2004).

In this article: Deuterium depleted low viscosity single layer interfacial metabolic water "floods" natural nanoindentations (A; red arrows) of the ATP synthase protein as a natural lubricant, produced from low deuterium ketogenic substrates during complete oxidation, matrix water production, oxygen utilization and Complex-IV activity in mitochondria.



www.CignatureHealth.com

ATP synthase movie


COMPUWARE
63


RPM/1000
km/h
HEADLAMPS SUGGESTED

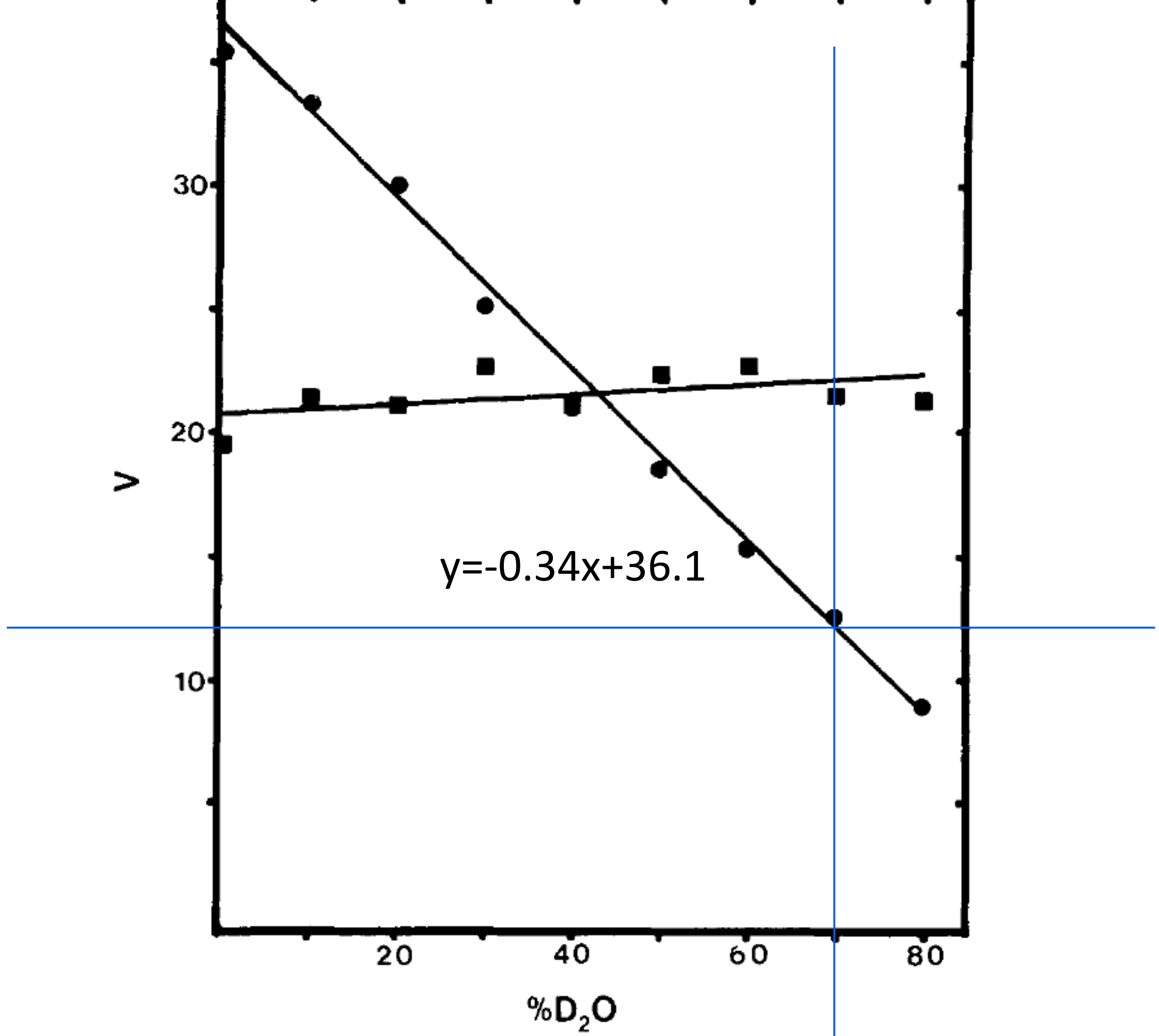


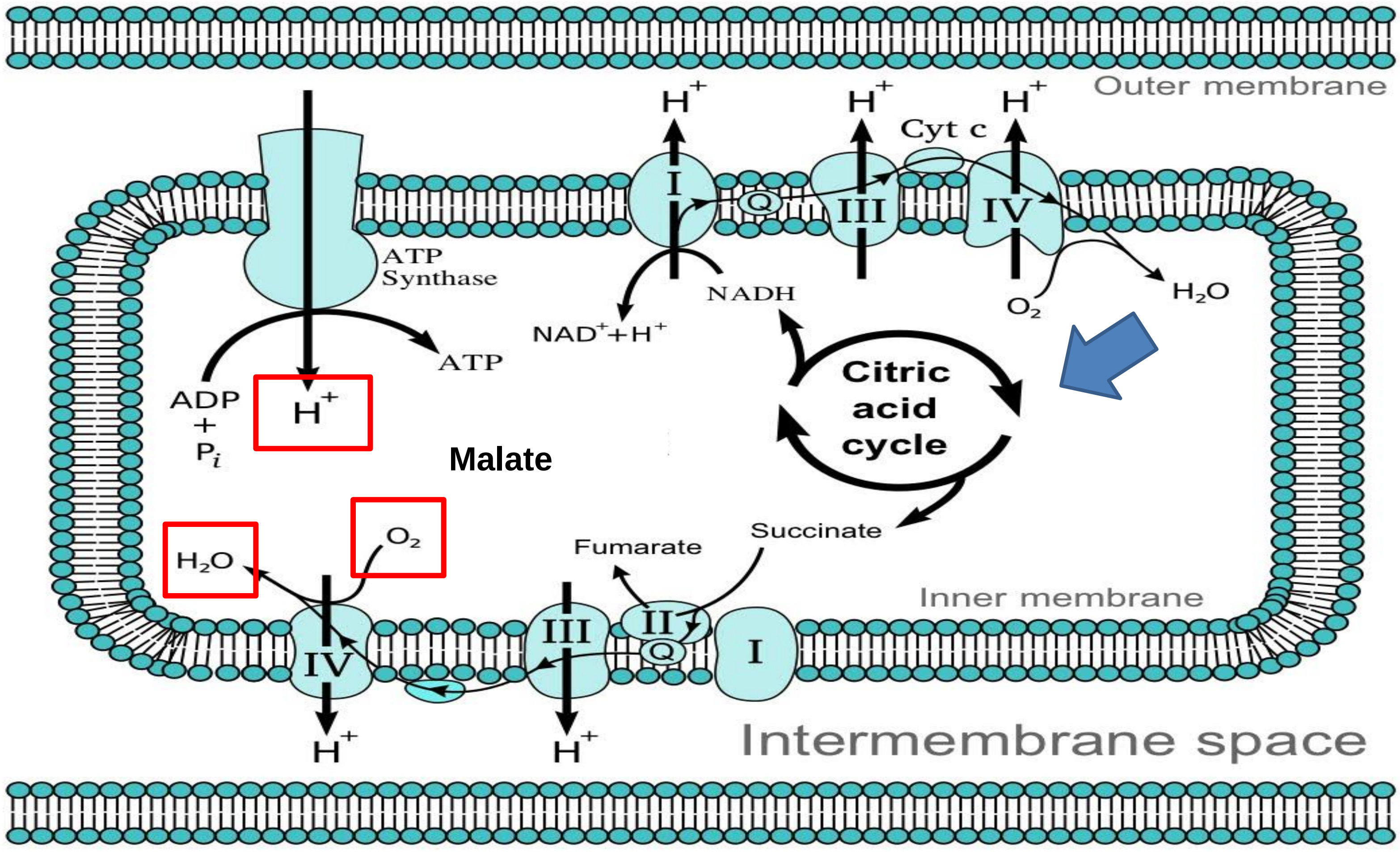
FIG. 2. **Effect of D_2O on the rate (in micromoles/min/mg) of ATP (●) and ITP (■) hydrolyses by native F_1.** Nucleotide concentration is 5 mM.

Dorgan LJ, Schuster SM. **The effect of nitration and D2O on the kinetics of beef heart mitochondrial adenosine triphosphatase.** J Biol Chem. 1981 Apr 25;256(8):3910-6.

Cytoplasmic water is what we drink and supply through circulation

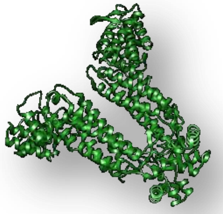
http://asiancorrespondent.com/92292/survey-what-worries-asias-kids/

MITOCHONDRIAL WATER IS WHAT IS PRODUCED IN THE MITOCHONDRIAL MATRIX

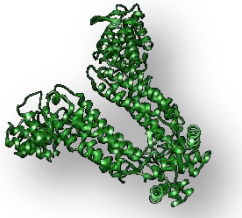


http://high-fat-nutrition.blogspot.com/2012/07/protons-wheres-bias.html

VCell TCA cycle
Movie and popcorn
(with butter and salt)



AMOUNTS AND PROPERTIES OF METABOLIC WATER PRODUCED IN MITOCHONDRIA DEPEND ON THE SUBSTRATES BEING OXIDIZED

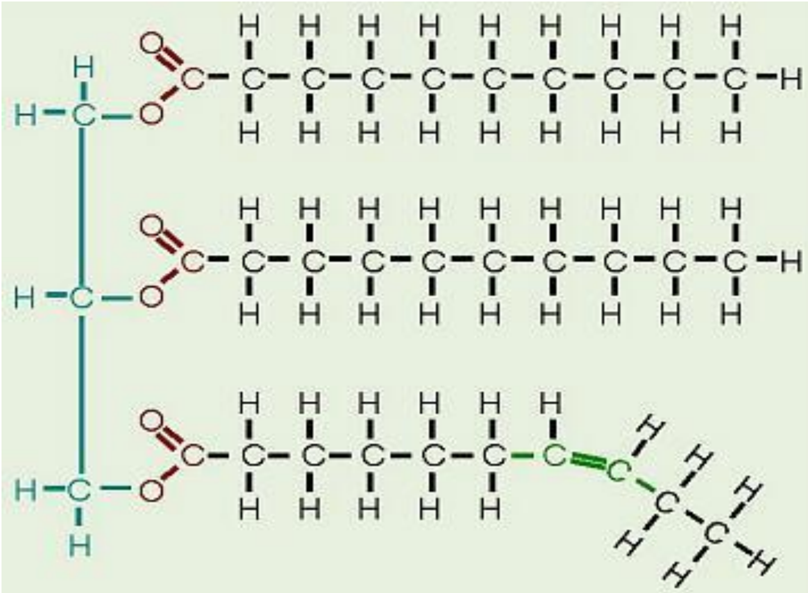


Nature 150, 21-21 (04 July 1942) | doi:10.1038/150021a0

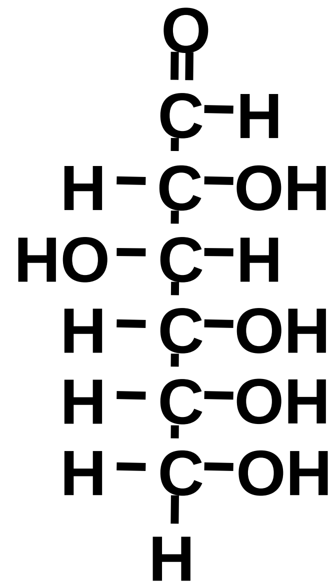
Metabolic Water and Desiccation

KENNETH MELLANBY

THE utilization by the body of ingested food substances and of tissue reserves yields among other things quantities of metabolic water. As the complete combustion of 100 gm. of fat produces about 110 gm. of metabolic water, whereas 100 gm. of carbohydrate yields only 55 gm. of water, fat reserves and fatty foods are believed to be particularly valuable as a protection against desiccation. This contention would appear to be supported by the fact that many animals which exist in deserts have large reserves of fat.

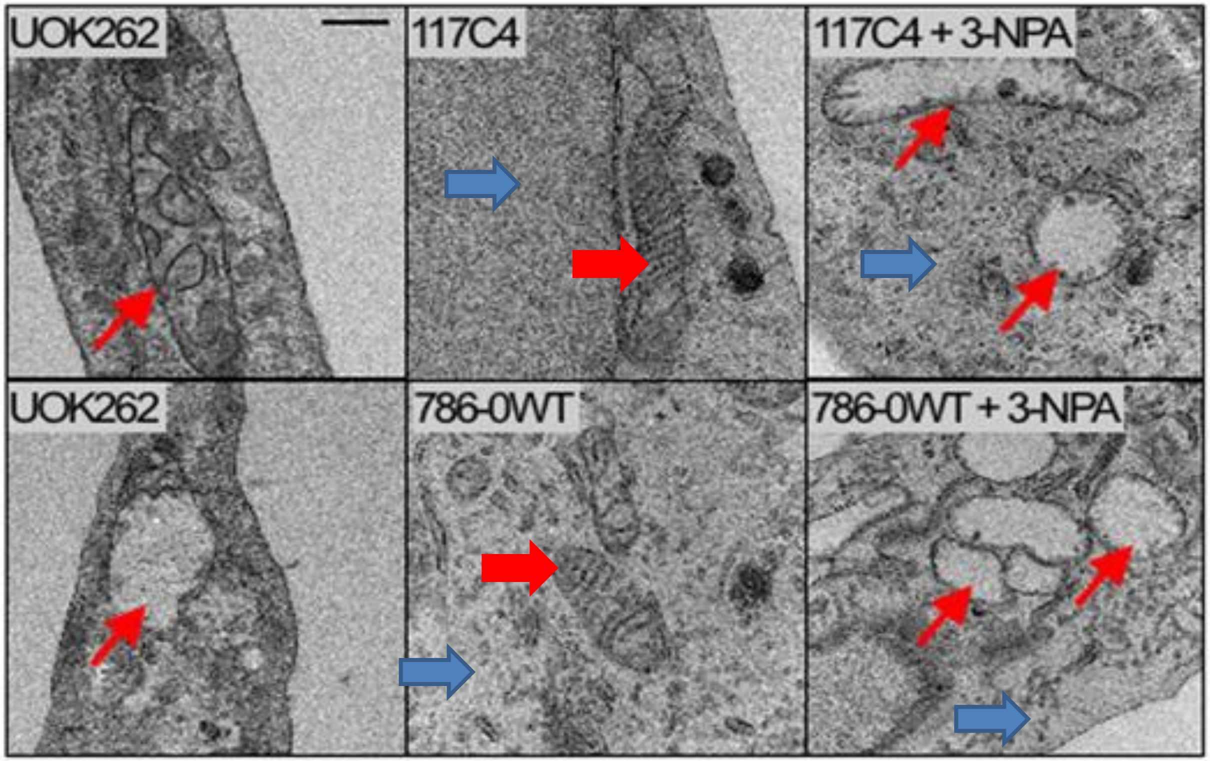


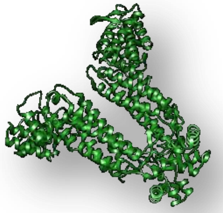
http://study.com/academy/lesson/what-is-fatty-acid-composition-structure-quiz.html



D-glucose

MITOCHONDRIAL AND CYTOPLASMIC
WATER POOLS IN CANCER





Let’s produce water by oxidation of substrates using different food constituents

Let’s turn the laboratory into “mitochondria”

This method will be transferred to USF

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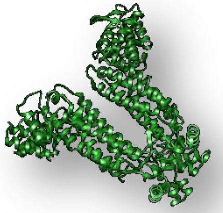
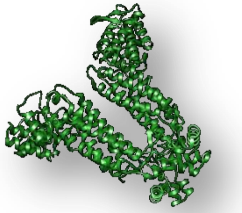
LABIOMED
HYD, LLC – MTA Geochemistry
SiDMAP, LLC



Methods I. (CuO catalysis)

- Five mg samples are placed in Pyrex glass tubes and covered by 1 cm Copper(II) oxide (CuO) bead columns and dried under vacuum in batches of n=8 for at least 30 minutes (10^{-3} bar)
- Samples are completely oxidized in a 500 °C oven for 16 hours (Coleman-method) – this is what happens in mitochondria and complex-IV
- The CuO slowly oxidizes all organic materials during the 16-hour period, followed by slow cooling down to room temperature
- One hundred mg zinc catalyst10 is measured in sealed Teflon tubes where water from the Pyrex tubes is carried by freezing at -80 °C – this is what fumarate hydratase does -, while the CO2 product of complete substrate oxidation was removed by vacuum (cryogen separation) – this is what we exhale through the lungs



Methods II. (IRMS)

- Frozen water onto Zinc is reduced by Zn catalysis in 30 minutes in 500 °C ovens to H_2 gas - this is what we transfer to NADP+
- ^2H (D) - ^1H ratio measurement using isotope ratio mass spectrometry (IRMS)
- Hydrogen gas using 2 microliter injections was loaded into the inlet of a Finnigan MAT delta S mass spectrometer at the Institute for Geological & Geochemical Research, Hungarian Academy of Sciences, Budapest, Hungary (Dr. István Fórizs)
- $^2H_1$ (D_1) concentrations (ppm) were calculated from the hydrogen's isotope composition

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Methods III. (laser spectroscopy)

- **Three laser spectroscope-validated BWS1, BWS2 and BWS3 laboratory standards, as well as one 29 ppm ^{2}H-containing water sample (supplied by the vendor) were prepared the same way with the samples to control for recovery and guide calculations**

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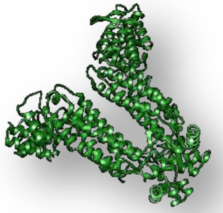
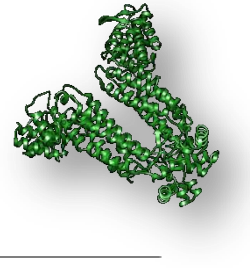


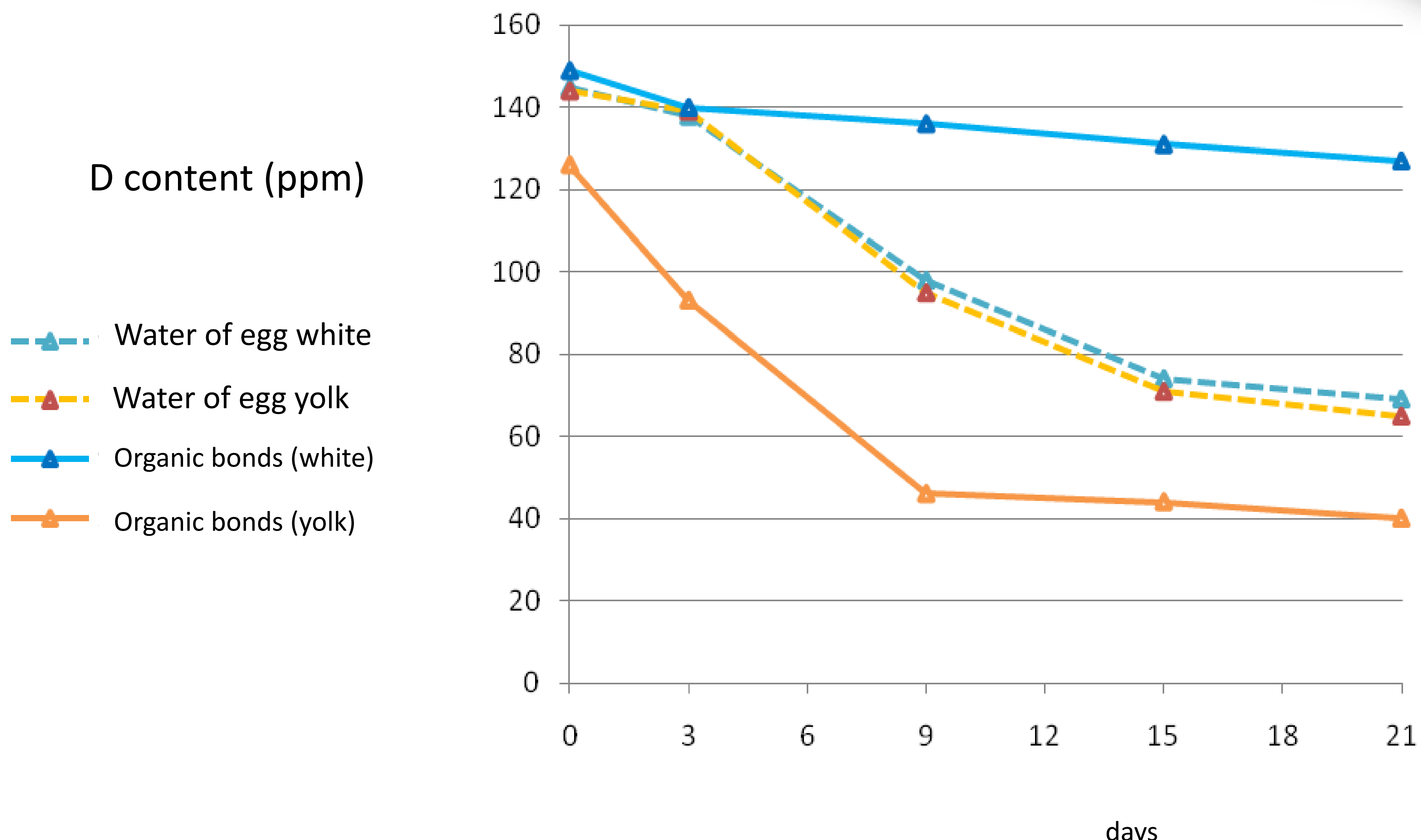
Methods IV. (δ^2H)

- **Sample and standard isotopic compositions are expressed as δ^2H values relative to V-SMOW according to the equation: $\delta = ((^2H/^1H\text{-sample} - {}^2H/^1H\text{-standard}) / (^2H/^1H\text{-standard}) \times 1000$ (‰), where $^2H/^1H$ ratios derive from either the sample or from the international standard of the European Atomic Energy Agency**

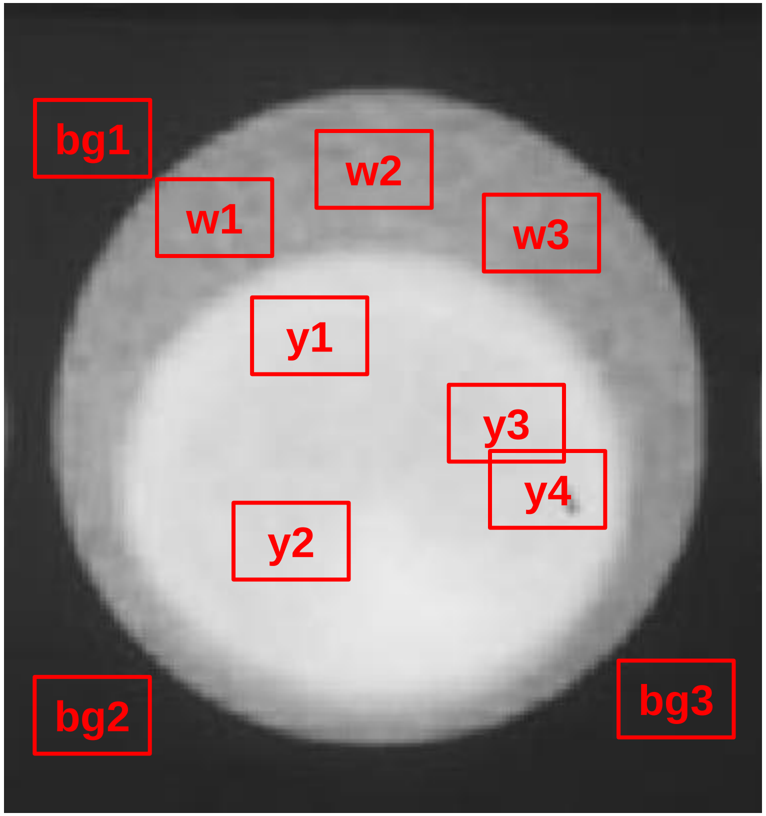
- **The precision of deuterium concentration ratios is less than 1.5 ppm based on duplicate (repeated) injections of samples**

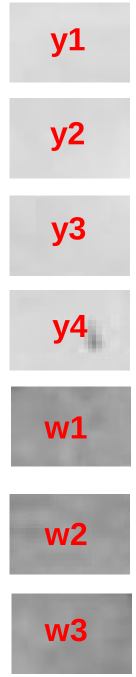
Deuterium content in eggs laid by 25 ppm DDW drinking hens





T1-WEIGHTED FRESH EGG





		T1 fresh egg		
samples	**variable**	**avg**	**min**	**max**
white1	rgb	157	123	171
	hsb	62	48	67
white2	rgb	155	139	168
	hsb	61	55	66
white3	rgb	153	108	171
	hsb	60	42	67
yolk1	rgb	218	212	224
	hsb	86	83	88
yolk2	rgb	217	211	229
	hsb	85	83	90
yolk3	rgb	213	206	223
	hsb	84	81	87
yolk4	rgb	213	137	226
	hsb	84	54	89
bg1	rgb	47	45	51
	hsb	18	18	20
bg2	rgb	41	38	49
	hsb	16	15	19
bg3	rgb	38	36	40
	hsb	15	14	16

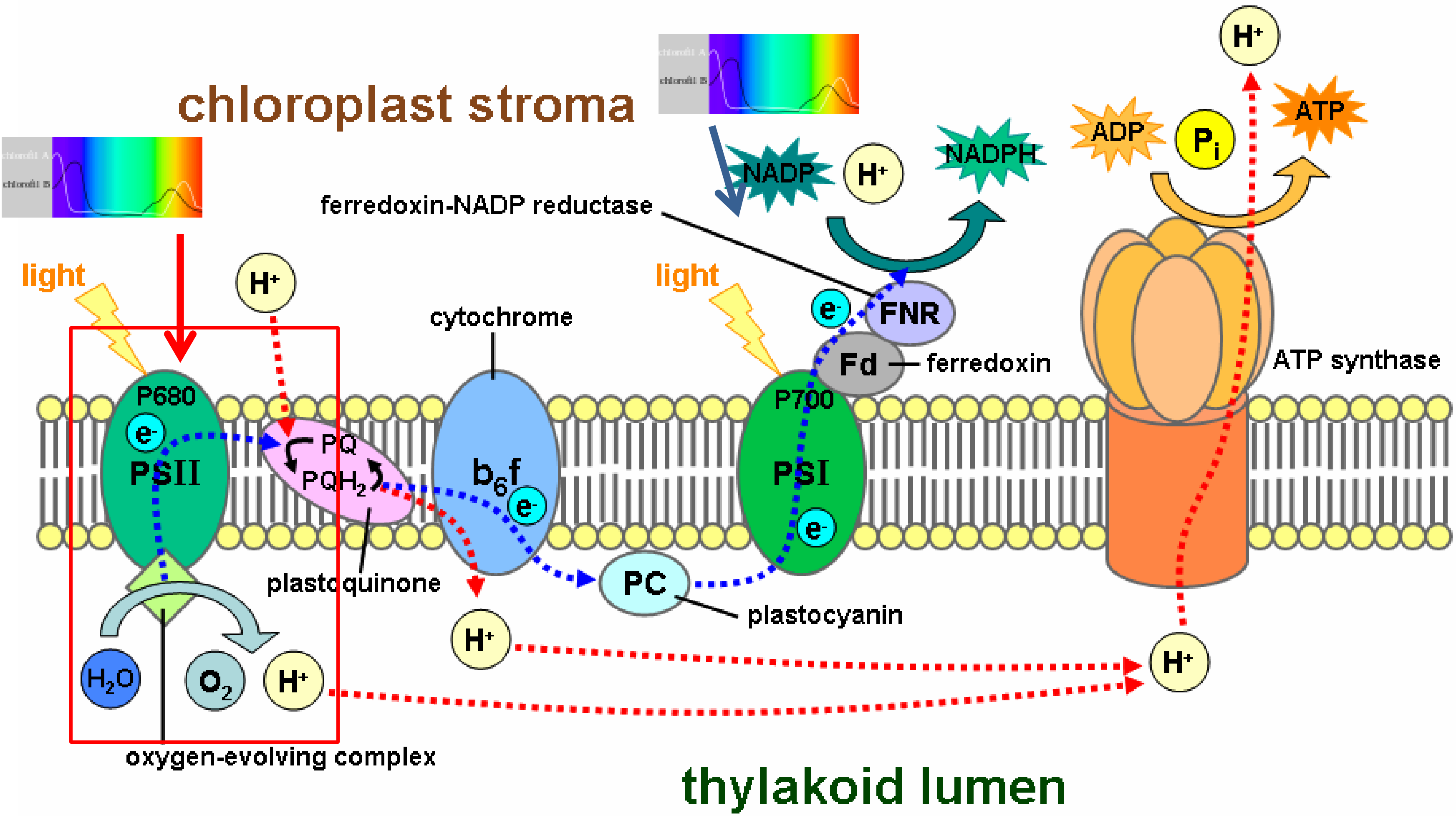
Size of samples: 60x40 pixel

(1.59x1.06 cm)

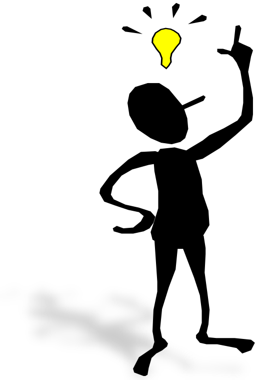
Source: AJNR Am J Neuroradiol 21:1470–1477, September 2000

Mitochondrial water is deuterium depleted and its low deuterium/hydrogen moiety originates from animal fat and green plant sugars by deuterium discrimination during photosynthesis

Photosystem II - water-plastoquinone oxidoreductase



Mitochondrial water is deuterium depleted and its low deuterium/hydrogen moiety shows up in fat/DNA by reductive synthesis



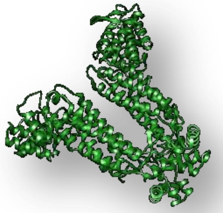
Hydrogen and deuterium have different physical/chemical properties in organic chemistry

-

Can deuterium shield protons on MRI and alter longitudinal (thermal) proton relaxation properties

break

7x slower



Single deuterium replacement disrupts collective proton tunneling of 96 other hydrogen molecules in hexagonal ice

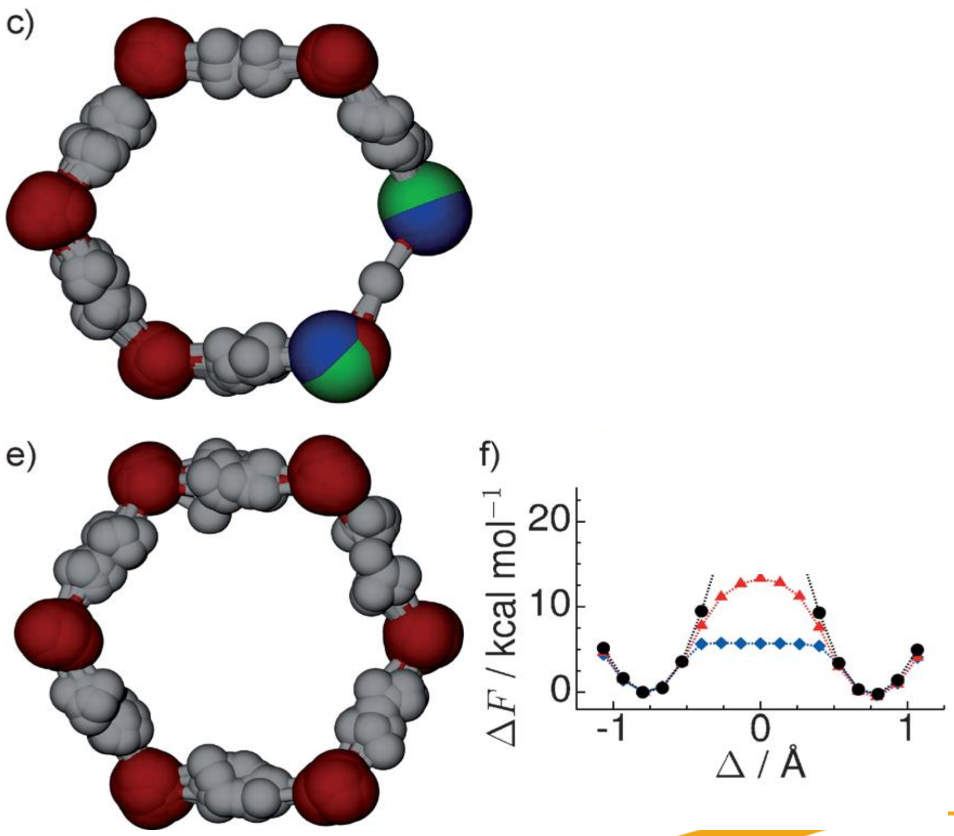
Exceptional Isotopic-Substitution Effect: Breakdown of Collective Proton Tunneling in Hexagonal Ice due to Partial Deuteration

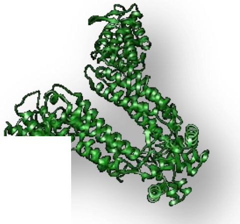
Christof Drechsel-Grau and Dominik Marx

DOI: 10.1002/anie.201405989

Angewandte Chemie

Single deuterium replacement disrupts collective proton tunneling of 96 other hydrogen molecules in hexagonal ice





Interfacial water of cells and mitochondria

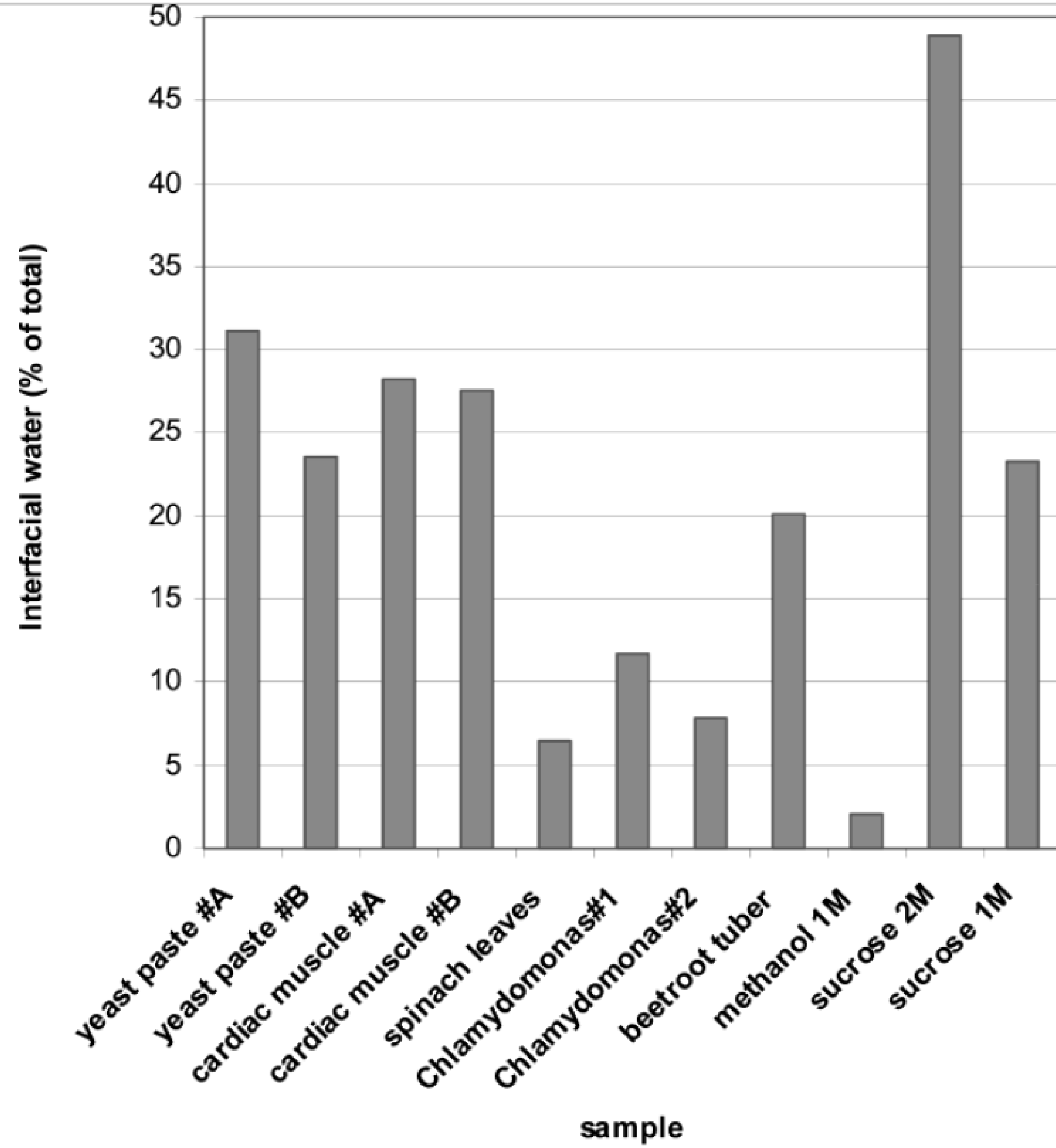
J|A|C|S
ARTICLES
Published on Web 03/19/2004

Inelastic Incoherent Neutron Scattering Measurements of Intact Cells and Tissues and Detection of Interfacial Water

Robert C. Ford,[*,†] Stuart V. Ruffle,[‡] Anibal J. Ramirez-Cuesta,[§] Ilias Michalarias,[#] Ilir Beta,[#] Aline Miller,[||] and Jichen Li[#]

Contribution from the Departments of Biomolecular Sciences, Physics, and Chemical Engineering, UMIST, Manchester M60 1QD, U.K., School of Biological and Chemical Sciences, University of Exeter, Exeter EX4 4QG, U.K., and ISIS, Rutherford Appleton Laboratory, Chilton, Didcot, Oxfordshire, OX11 0QX, U.K.

Received October 30, 2003; E-mail: r.ford@umist.ac.uk



Summary of the relative interfacial water content in the different cells and tissues surveyed, and a comparison to standard solutions of small
: interfacial water signal in the librational region of the IINS spectrum (45−130 meV) was integrated and then expressed as a percentage of the

In conclusion, we previously[5] predicted that the interfacial water content in cells and tissues could represent a significant fraction of the total water, and in some cases (e.g., in mitochondria) could approach 100% of the water. We have now tested this prediction experimentally using IINS. An estimate of ~25−30% of water as interfacial was obtained from the data for yeast and cardiac cells. We expect this to be somewhat lower

Every interchange of 1% of the H for D gives a rate change of 0.35 > micromoles/min/mg (close to a percent of the rate at 0% D)

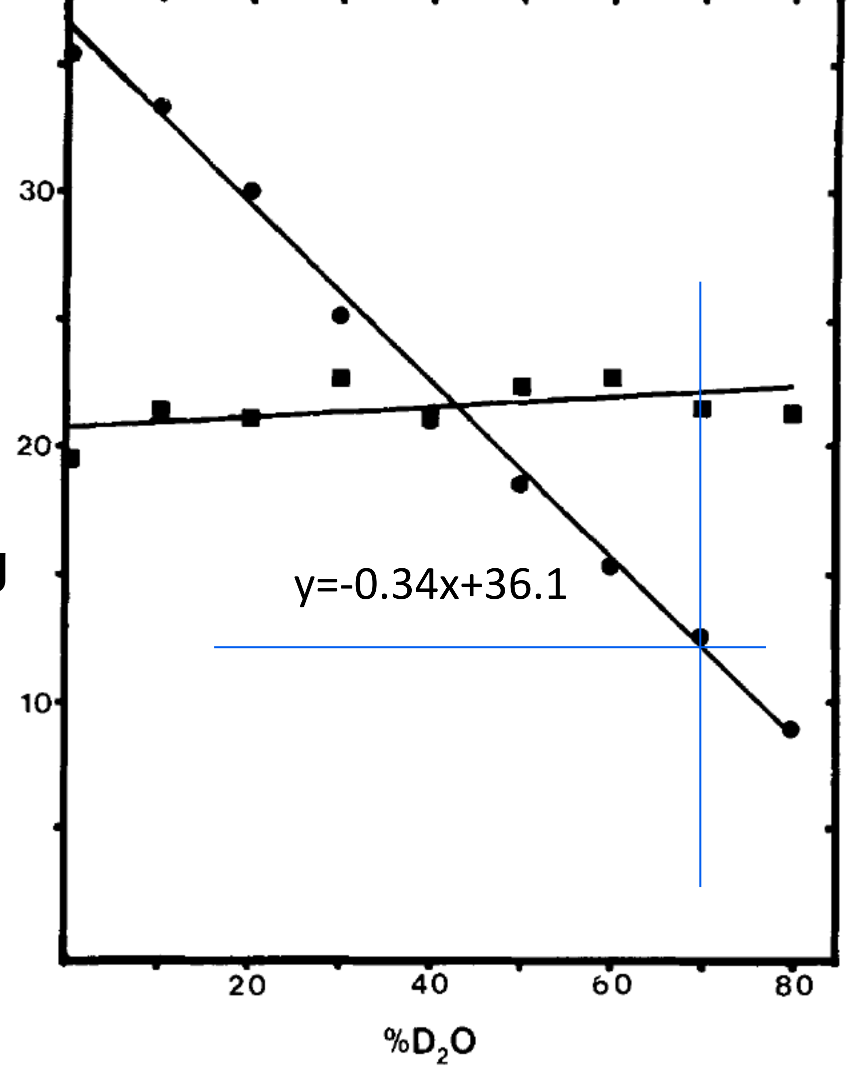


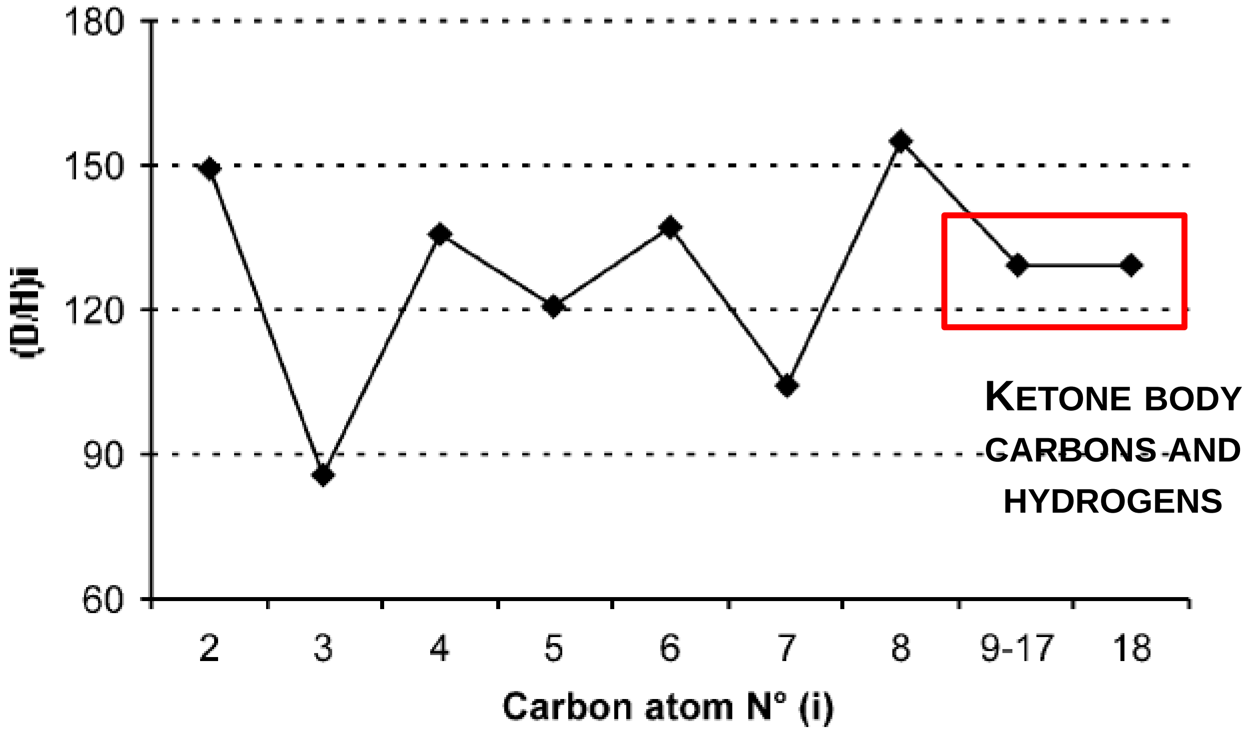
FIG. 2. **Effect of D_2O on the rate (in micromoles/min/mg) of ATP (●) and ITP (■) hydrolyses by native F_1.** Nucleotide concentration is 5 mM.

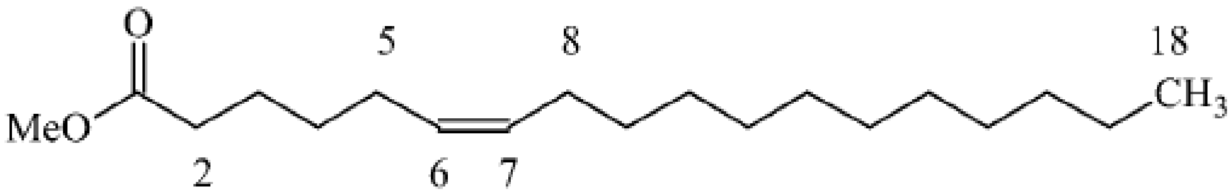
In deuterium free water the base ATP hydrolysis rate is calculated as **36.1** micromoles/min /mg in beef heart.

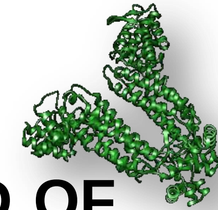
Dorgan LJ, Schuster SM. **The effect of nitration and D2O on the kinetics of beef heart mitochondrial adenosine triphosphatase.** J Biol Chem. 1981 Apr 25;256(8):3910-6.

Source	Substrate, nutrient y=-0.34x+36.1 micromoles/min/mg	Average deuterium content [% decrease]*	Calculated change in ATP hydrolysis** with (%) increase to maximum rate***	Increase in ATP synthesis as the function of carbohydrate (flour) deriving metabolic water
Water (mean ocean water)	International Atomic Energy Agency Standard	155.8 [Reference range - N/A]	+0	N/A
Water of cottage cheese (distilled by freezing under vacuum)	water from curd cheese - Quark dairy product	151 [-3.1]	+1.1** (3.04)***	0.8
Flour	wheat dehydrated all-purpose PN-A-74022:2003	150 [-3.8]	+1.3 (3.6)	1 (Reference)
Table sugar	sucrose – Culinary white refined (CAS 57-50-1)	146 [-6.3]	+2.1 (5.8)	1.6
Cottage cheese (dry)	curd - Quark dairy product	136 [-12.7]	+4.3 (11.9)	3.3
Sunflower oil with ~84% high oleic acid variety	From Helianthus annus seeds	130 [-16.6]	+5.6 (15.5)	4.3
Butter	From cows' milk	124 [-20.4]	+6.9 (19.1)	5.3
Pork fat	Wet-rendered lard - pork fatback	118 [-24.3]	+8.3 (22.9)	6.4

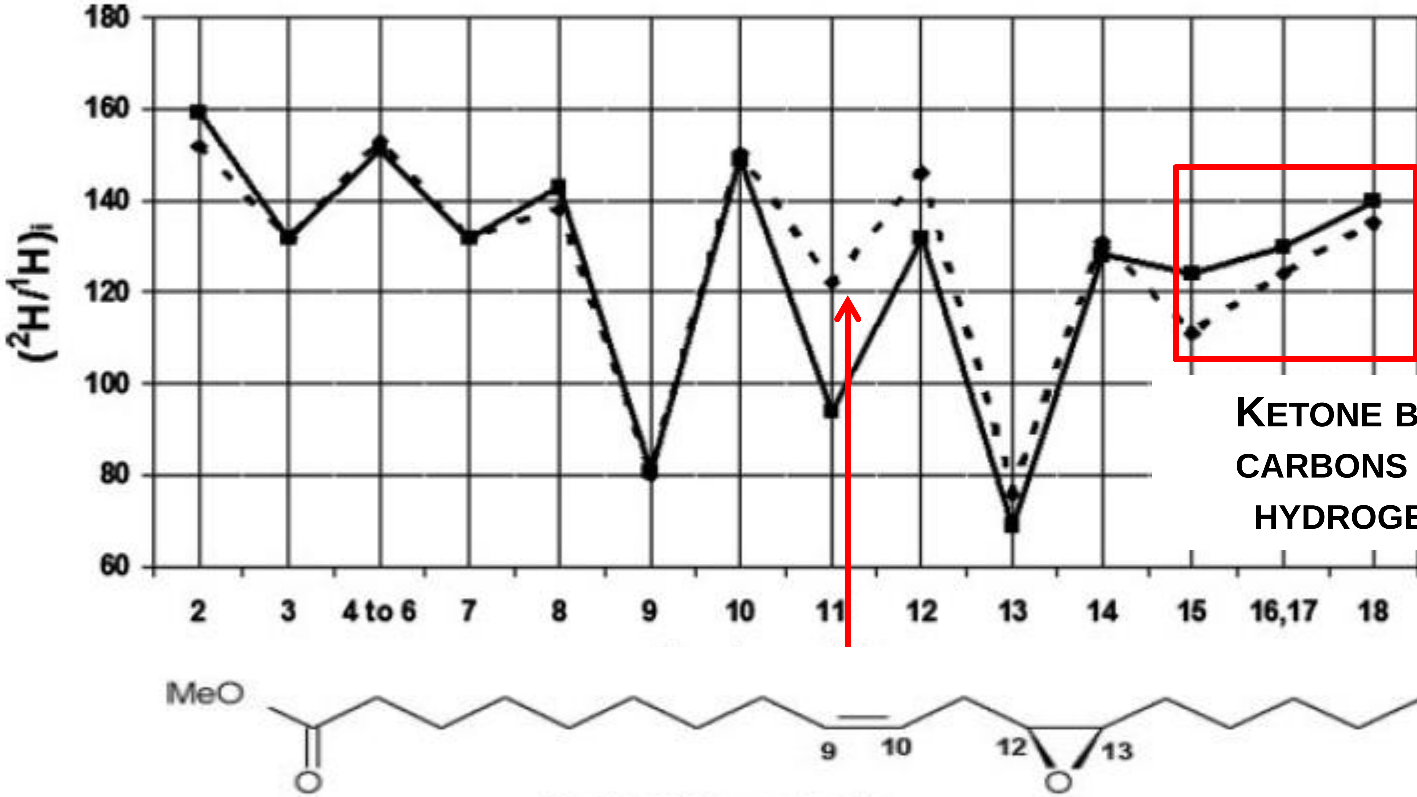
DOUBLE BONDS ARE ALMOST ALWAYS DEPLETED OF DEUTERIUM IN BIOLOGY (PARSLEY SEED)







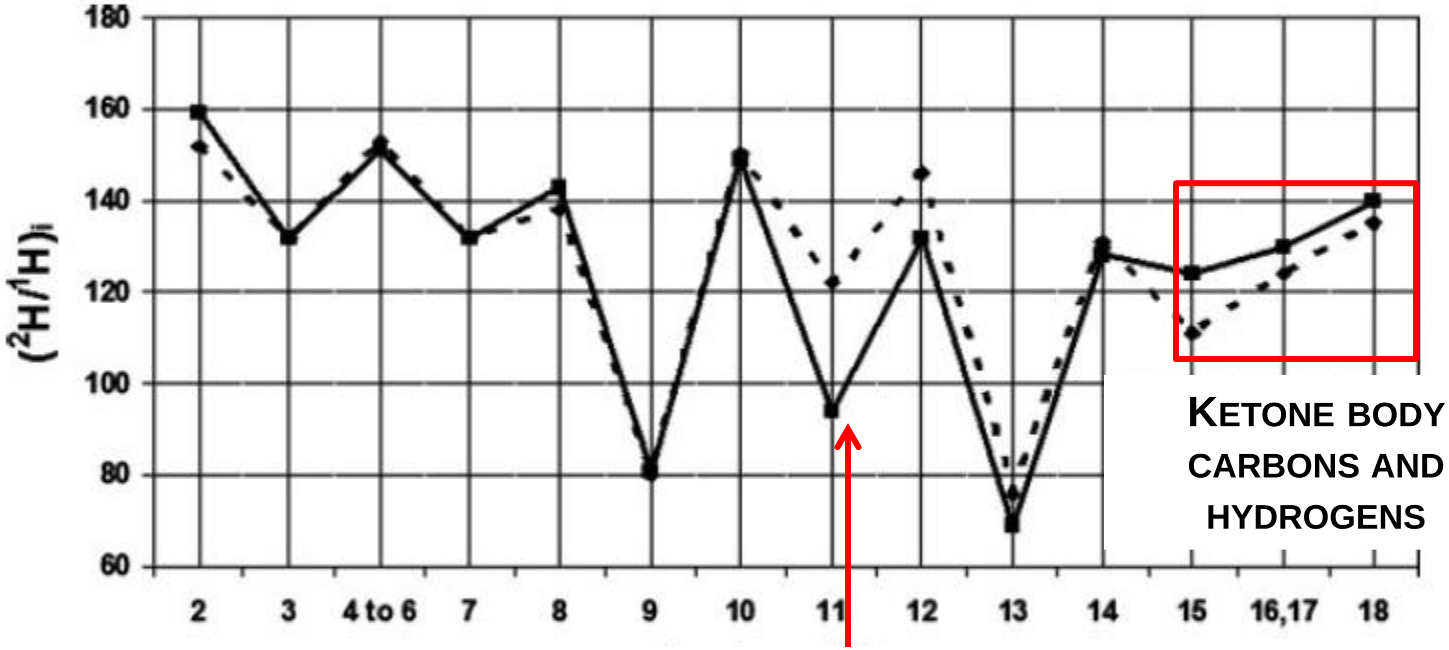
DOUBLE BONDS ARE ALMOST ALWAYS DEPLETED OF DEUTERIUM IN BIOLOGY (IRONWEED SEED)

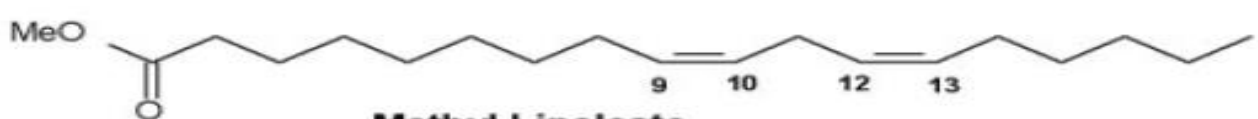


Methyl Vernoleate
1

JBC 280, 17645–17651, 2005

DOUBLE BONDS ARE ALMOST ALWAYS DEPLETED OF DEUTERIUM IN BIOLOGY (IRONWEED SEED)

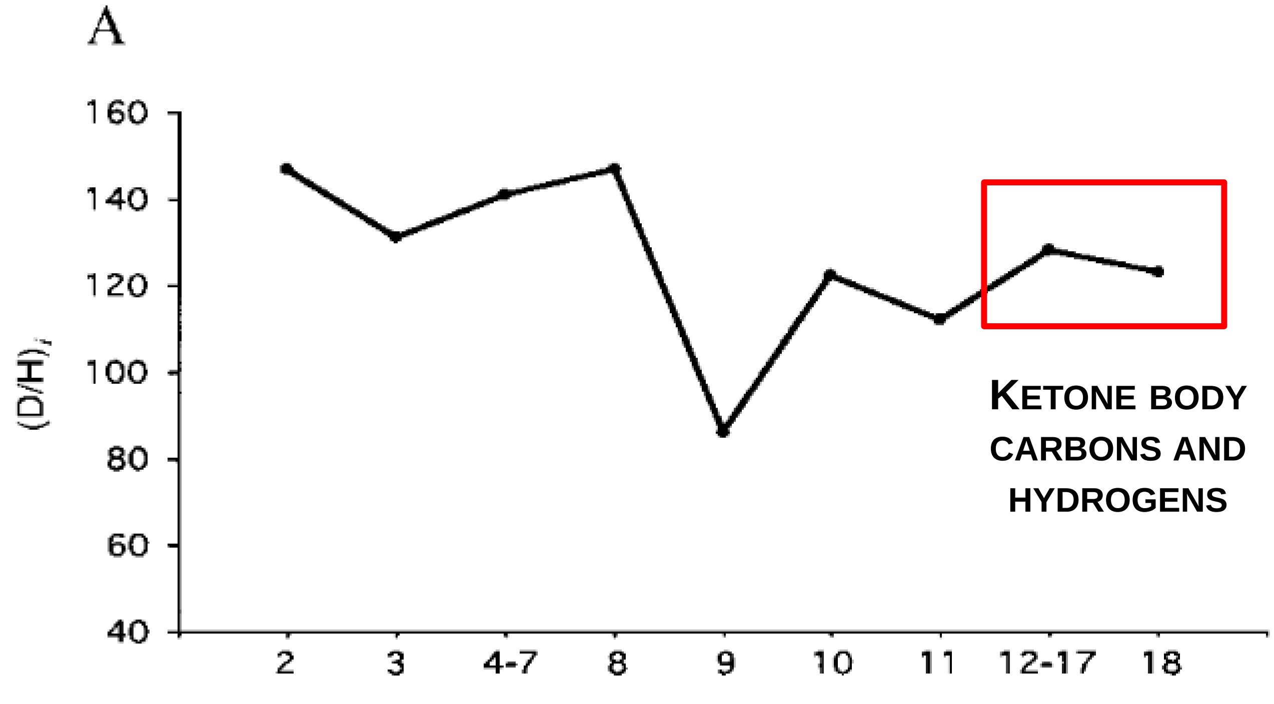


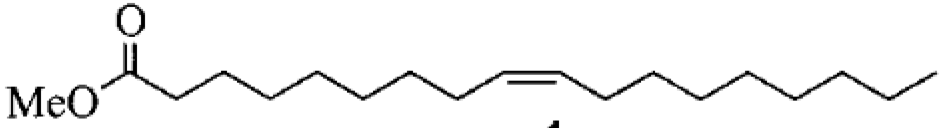


Methyl Linoleate
2

JBC 280, 17645–17651, 2005

DOUBLE BONDS ARE ALMOST ALWAYS DEPLETED OF DEUTERIUM IN BIOLOGY (OLEATE - SUNFLOWER)

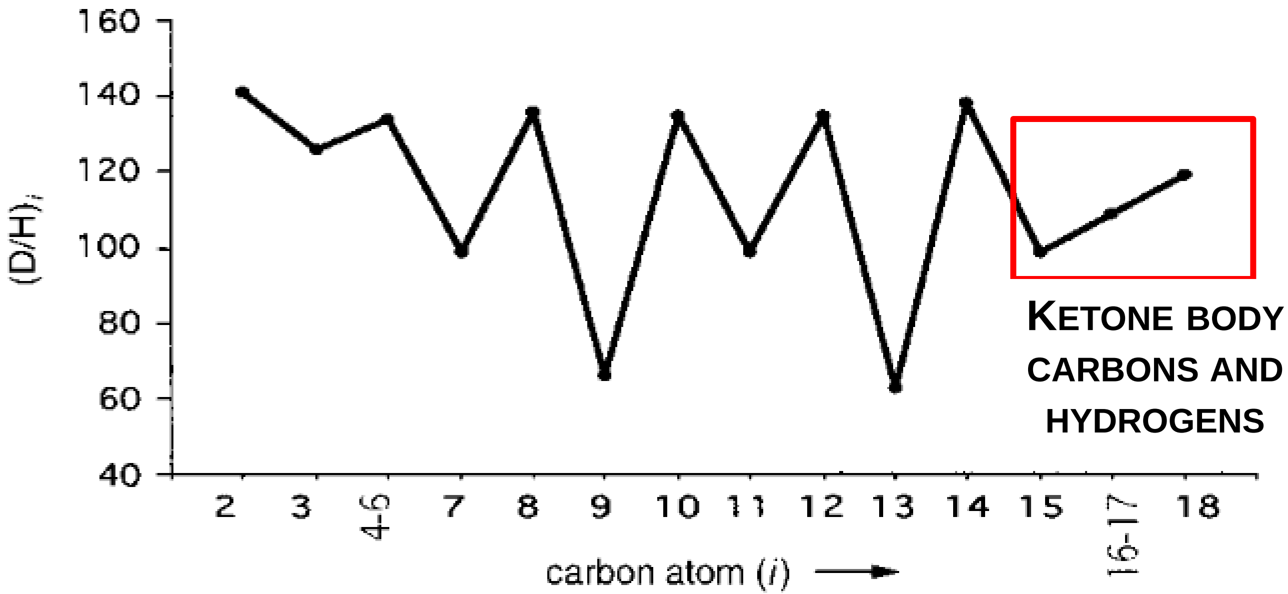


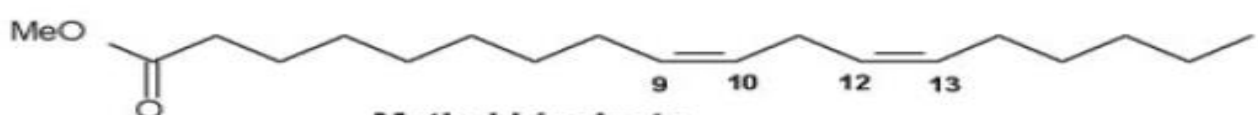


1

CHEMBIOCHEM 2001, 2, 425 ± 431

DOUBLE BONDS ARE ALMOST ALWAYS DEPLETED OF DEUTERIUM IN BIOLOGY (SUNFLOWER)





Methyl Linoleate
2

CHEMBIOCHEM 2001, 2, 425 ± 431

Source (Species)	Fatty acids, carbon clusters and fragments y=-0.34x+36.1 micromoles/min/mg	Average deuterium content [% decrease]*	Calculated change in ATP hydrolysis** with (%) increase to maximum rate***	References
Ironweed (Vernonia galamensis)	vernoleate linoleate	127.5 [-18.2%] 123.9 [-20.5%]	+6.2 (17.1) +6.8 (18.8)	Billault, I., et al. 2005. J. Biol. Chem. 280, 17645–17651.
Peanut oil (Arachis hypogaea)	palmitate and stearate (cluster C1-C7)	119.9 [-23.1%]	+7.9 (21.9)	Duan, J.R., et al. 2002. ChemBioChem. 3, 752–759.
Sunflower (Helianthus annus)	linoleate (cluster C13-C18) terminal ketones	110 [-29.7%]	+10.1 (27.7)	Billault, I., et. al. 2001. ChemBioChem 2, 425–431.
Parsley seed (Petroselinum crispum)	petroselinic acid ($C18:1D^6$) y=-0.34x+36.1	124.9 [-19.9%]	+6.8 (18.8)	Guiet, S., et al. 2003. Phytochemistry. 64, 227-33.

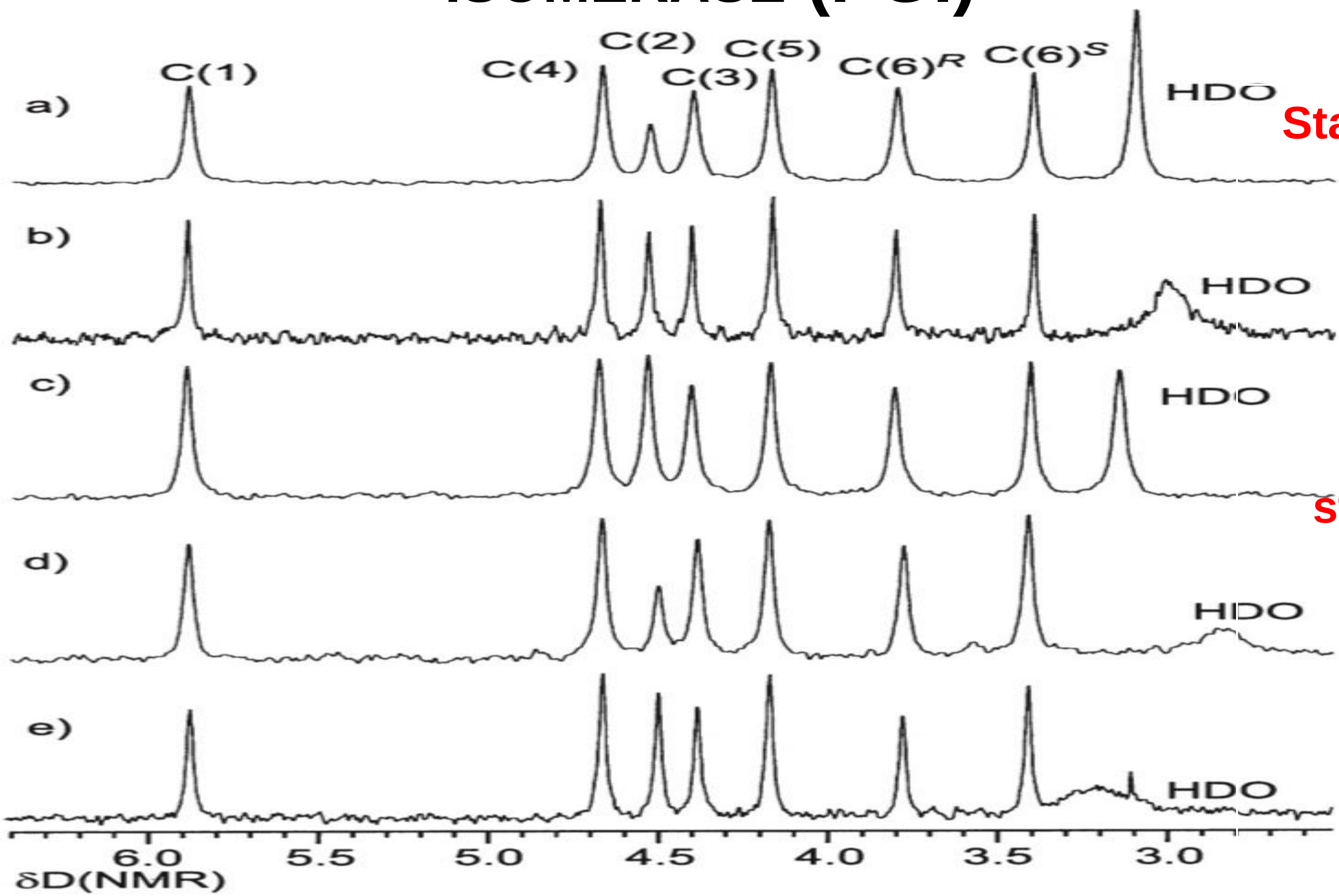
Plant, Cell & Environment
Volume 22, Issue 5, pages 525–533, May 1999

Intramolecular deuterium distributions reveal disequilibrium of chloroplast phosphoglucose isomerase

J. SCHLEUCHER, P. VANDERVEER, J. L. MARKLEY, T. D. SHARKEY

DOI: 10.1046/j.1365-3040.1999.00440.x

INTRAMOLECULAR DEUTERIUM DISTRIBUTIONS REVEAL DISEQUILIBRIUM OF CHLOROPLAST PHOSPHOGLUCOSE ISOMERASE (PGI)



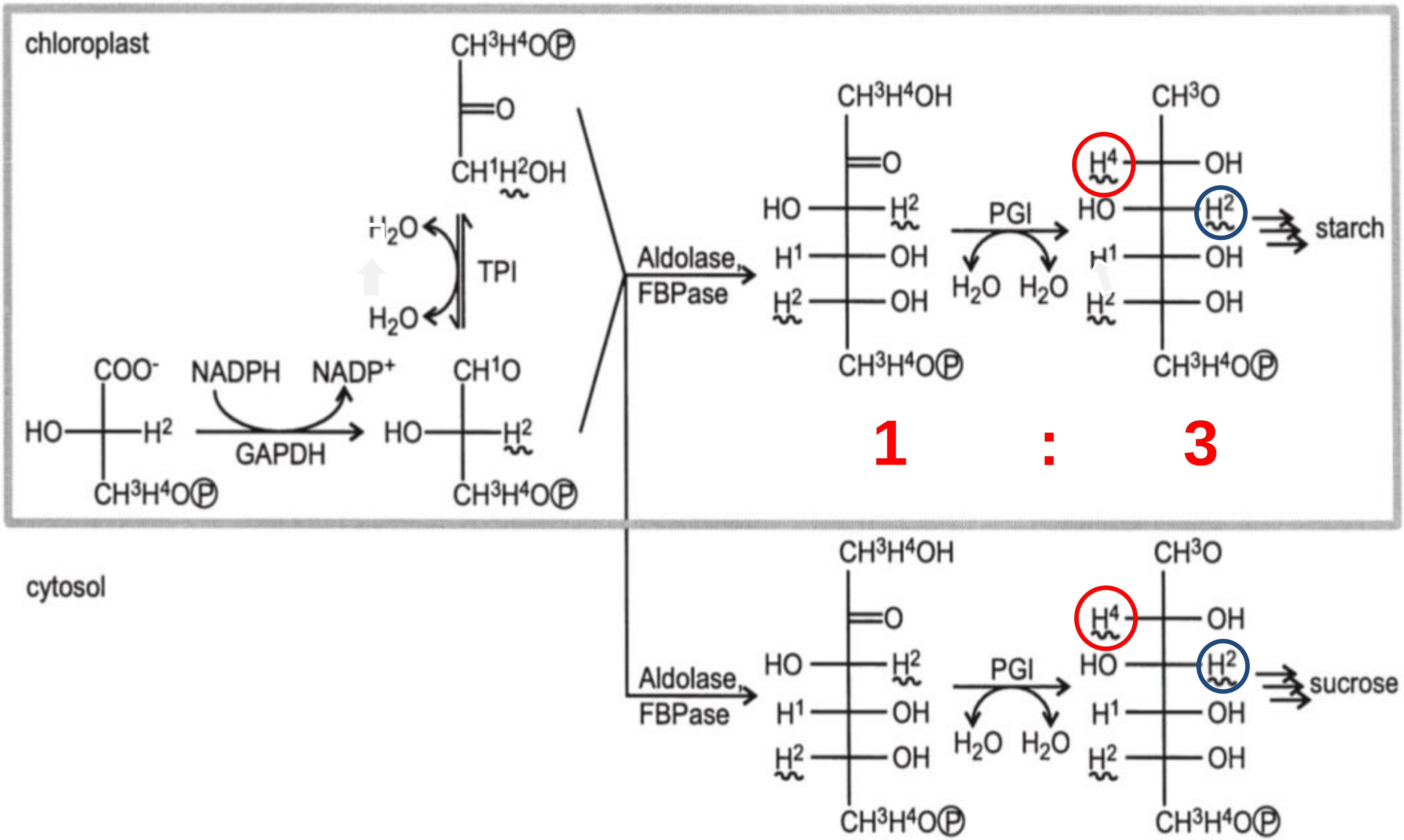
Starch (beans)

Sucrose (beans)

Endosperm starch (bean)

Starch (spinach)

Sucrose (spinach)


chloroplast
CH3H4OP
O
CH1H2OH
H2O
TPI
H2O
COO-
HO
H2
CH3H4OP
NADPH
NADP+
GAPDH
CH1O
HO
H2
CH3H4OP
Aldolase,
FBPase
CH3H4OH
O
HO
H2
H1
OH
H2
OH
CH3H4OP
PGI
H2O
H2O
CH3O
H4
OH
HO
H2
H1
OH
H2
OH
CH3H4OP
starch
1 : 3
cytosol
Aldolase,
FBPase
CH3H4OH
O
HO
H2
H1
OH
H2
OH
CH3H4OP
PGI
H2O
H2O
CH3O
H4
OH
HO
H2
H1
OH
H2
OH
CH3H4OP
sucrose

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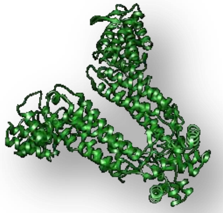

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