Nuclear Spin Catalysis in Biosystems: Premises and Promises

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VIII International Symposium

"Actual Problems of Biophysical Medicine",

Kyiv, Ukraine, May 14-17, 2014

Concept

Some chemical elements have two kinds of *stable isotopes, i.e. - magnetic* and *non-magnetic* isotopes

$^{12,13}C$, $^{16,17,18}O$, $^{24,25,26}Mg$, $^{28,29}Si$, $^{32,33,34}S$, $^{40,42,43,44,48}Ca$, $^{54,56,57,58}Fe$, $^{64,66,67,68}Zn$, $^{74,76,77,78,80,81}Se$, $^{92,94,95,96,97,98,100}Mo$

1. *Can living cells perceive the difference between magnetic* and *non-magnetic* *nuclei of the same element?*

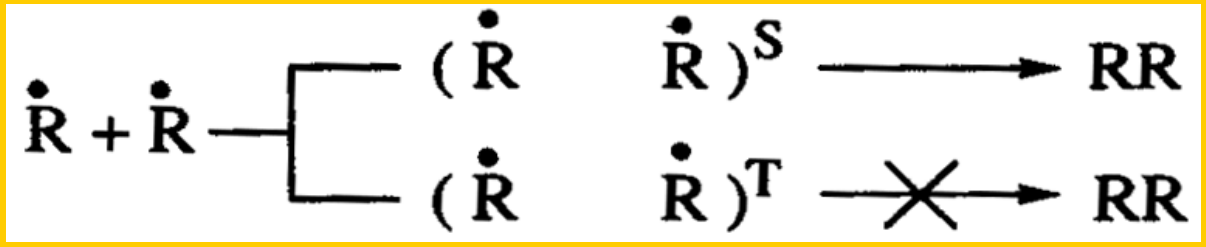
2. Stable magnetic isotopes to control over efficiency and reliability of cell nanoreactors?

Spin Chemistry

***Basis*: Apart from the law of conservation of energy, all chemical reactions obey the law of conservation of the spin angular momentum ('spin'). The reaction is rigorously forbidden if it requires a change in the total electron spin (S), namely, the total electron spin of products must be identical to the total electron spin of reactants.**

Spin Control of Chemical Reactions

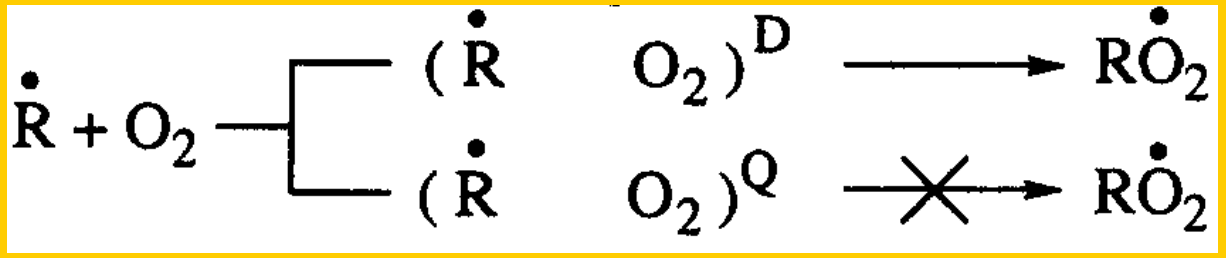
$S = 1$ or 0



$S = 0$

From 4 possible spin states of the radical pair, only singlet state is permitted for recombination into the diamagnetic molecule.

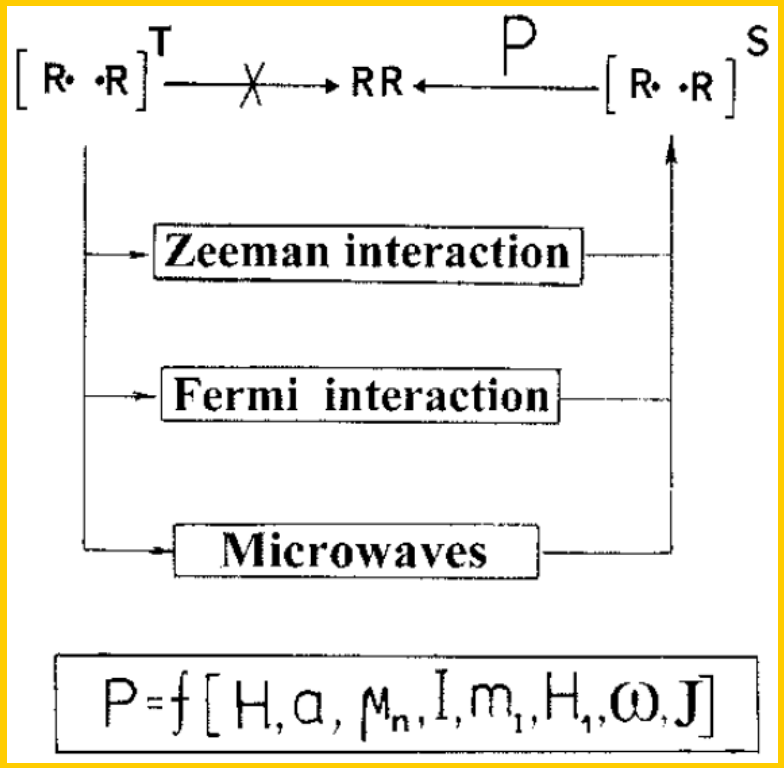
$S = 3/2$ or $1/2$



$S = 1/2$

From 6 possible spin states, only doublet spin states are permitted for synthesis of $\bullet RO_2$.

Spin Catalysis



Consequence **Acceleration of the free-radical reactions can be achieved by changing in the total electron spin of reactants via external magnetic fields, including magnetic fields of nuclear spins.**

Innovation **The free-radical reaction will show different reaction rates and different yields of products according to whether the reagents contain magnetic or nonmagnetic isotopes. That is known as 'magnetic isotope effect' (MIE).**

In action, MIE is purely a kinetic phenomenon and shows itself as the dependence of the reaction rate on the nuclear spins of the reactants.

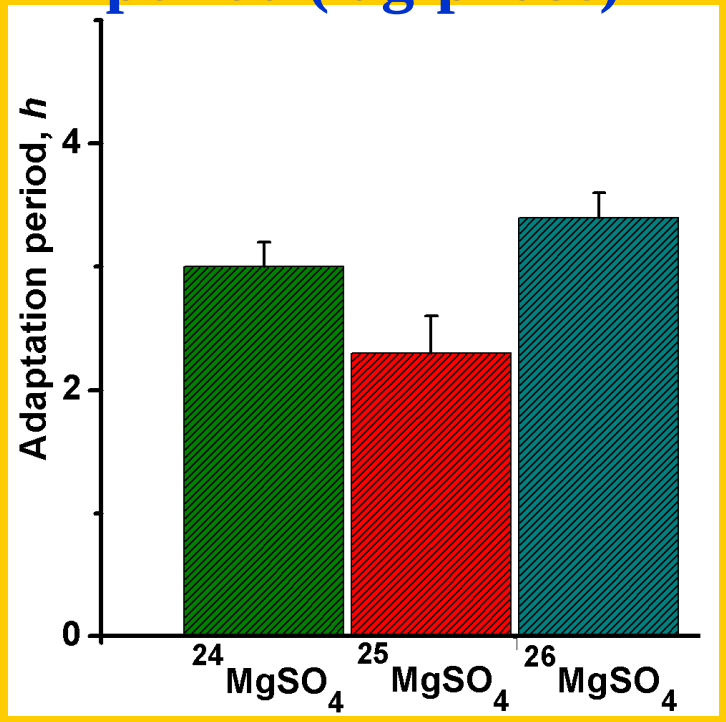
Mg^{2+} is main intracellular cation, obligatory cofactor of Mg^{2+}-dependent enzymes, including ATP-synthases, ATP-hydrolases, DNA-polymerases, ribonucleases, etc.

Three stable magnesium isotopes, ^{24}Mg, ^{25}Mg and ^{26}Mg with natural abundance about 79, 10 and 11%.

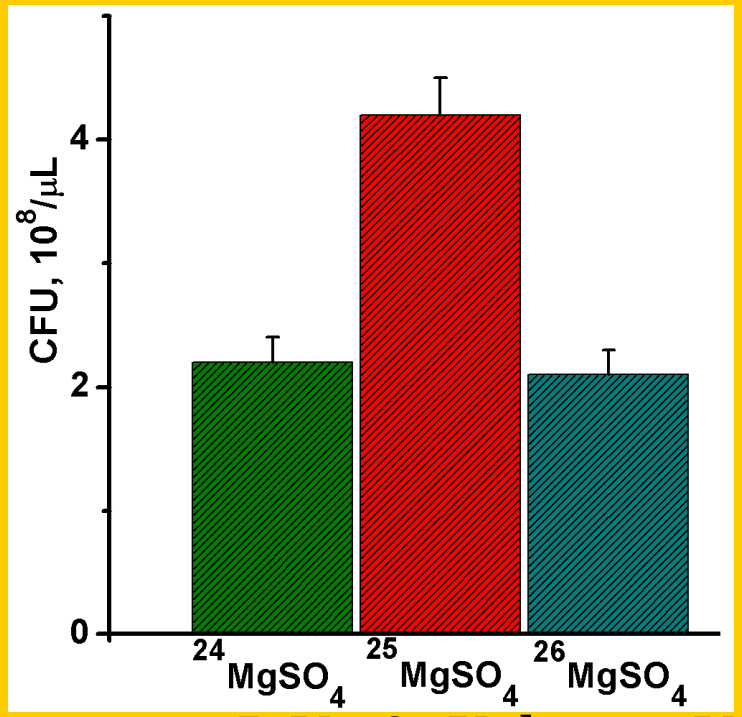
^{25}Mg has nuclear spin ($I = 5/2$).
^{24}Mg and ^{26}Mg have no spin ($I = 0$).

E. coli supplemented with different isotopes of magnesium

Length of the adaptation period (lag-phase)



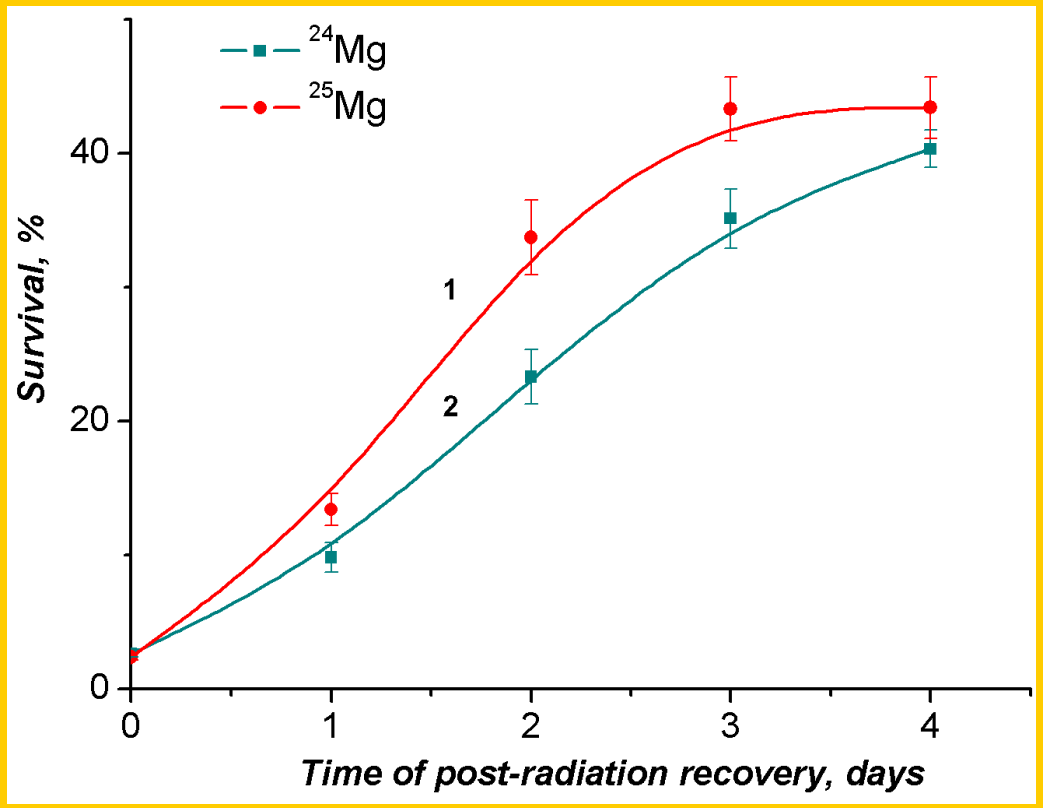
Colony-forming units on solid nutrient agar



Bogatyrenko, T.N., Kudryashova, E.A., Tumanova, L.V., & Koltover, V.K. ***Proceedings of the V International congress on Low and Superlow Fields and Radiations in Biology and Medicine*****, Saint-Petersburg, 2009, p. 92.**

Koltover, V.K., Shevchenko, U.G., Avdeeva, L.V., Royba, E.A., Berdinsky, V.L., & Kudryashova, E.A. ***Doklady Biochemistry and Biophysics*****, 2012, Vol. 442, No. 1-2, 12-14.**

Effect of magnetic ^{25}Mg isotope on postradiation recovery of *S. cerevisiae*, diploid strain, after *UV* irradiation

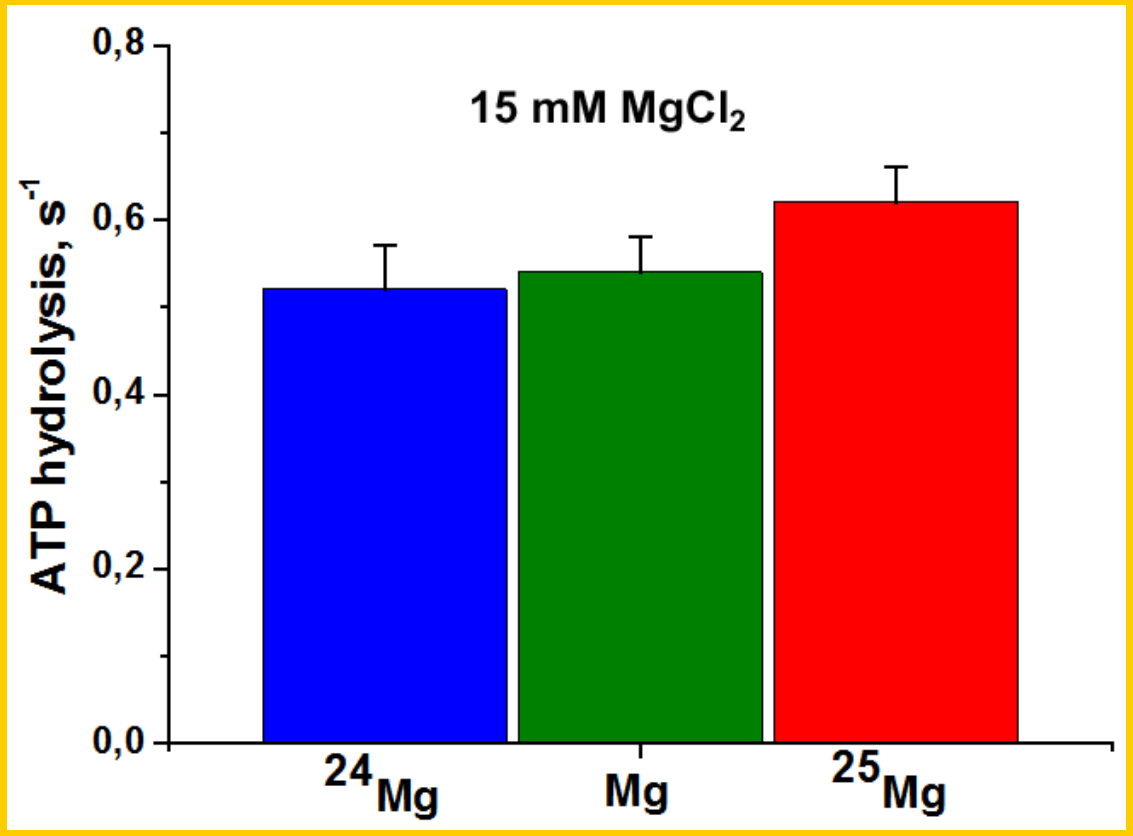


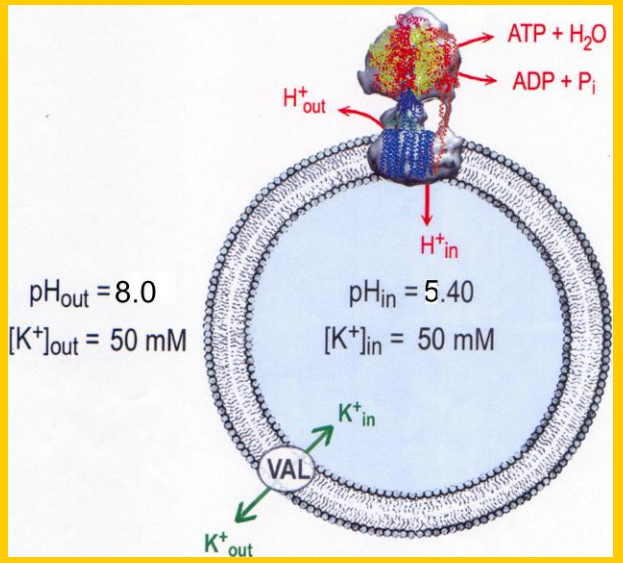
	β, h^{-1}	k
^{24}Mg	0.032 ± 0.003	0.70 ± 0.14
^{25}Mg	0.058 ± 0.004*	0.61 ± 0.12

*Difference of the means is significant at P=0.02 (N=3).

V.K. Koltover, V.G. Korolev, Y.A. Kutlakhmedov, In: *Ionizing Radiation: Applications, Sources and Biological Effects*, Nova Science, New York, 2012, pp. 117-128.

Hydrolysis of ATP by the purified yeast H^+-ATPase in proteoliposomes





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Vitaly Koltover, (IPCP, Russia)

Muscle myosin is among the key enzymes in cell bioenergetics. Nonmuscle myosin II powers myriad developmental and cellular processes, including embryogenesis, cell migration, and cytokinesis, etc.

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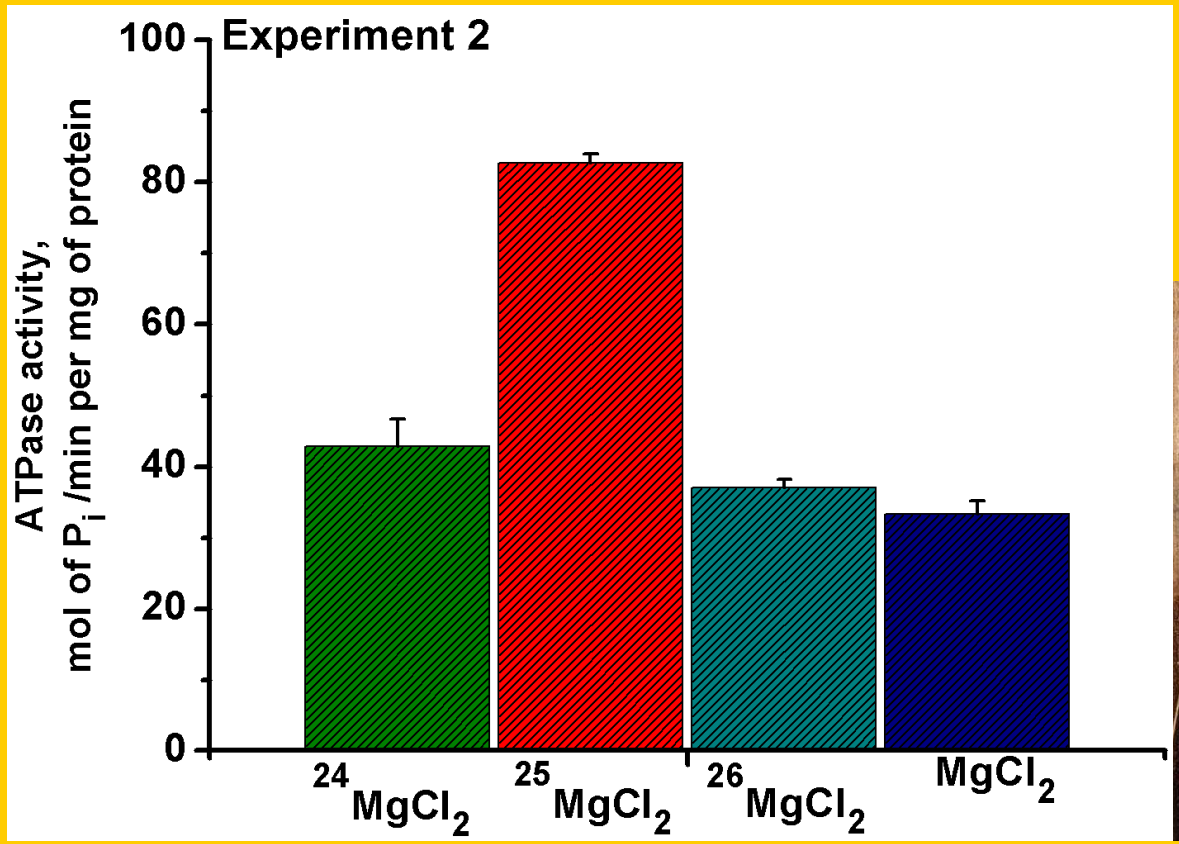
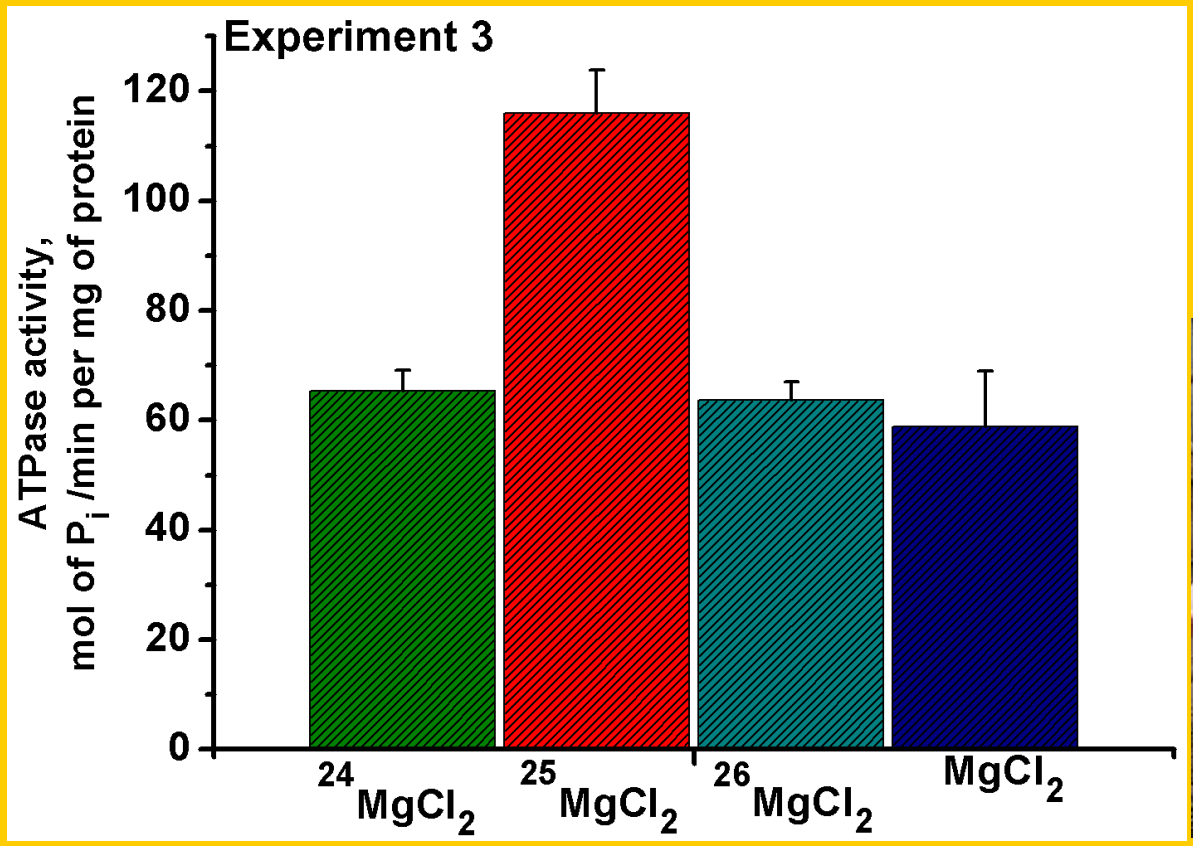
Effects of $^{25}MgCl_2$ (magnetic isotope, nuclear spin I=5/2), $^{24}MgCl_2$ (nonmagnetic, I=0) and $^{26}MgCl_2$ (nonmagnetic, I=0) on ATP hydrolysis catalyzed by myosin



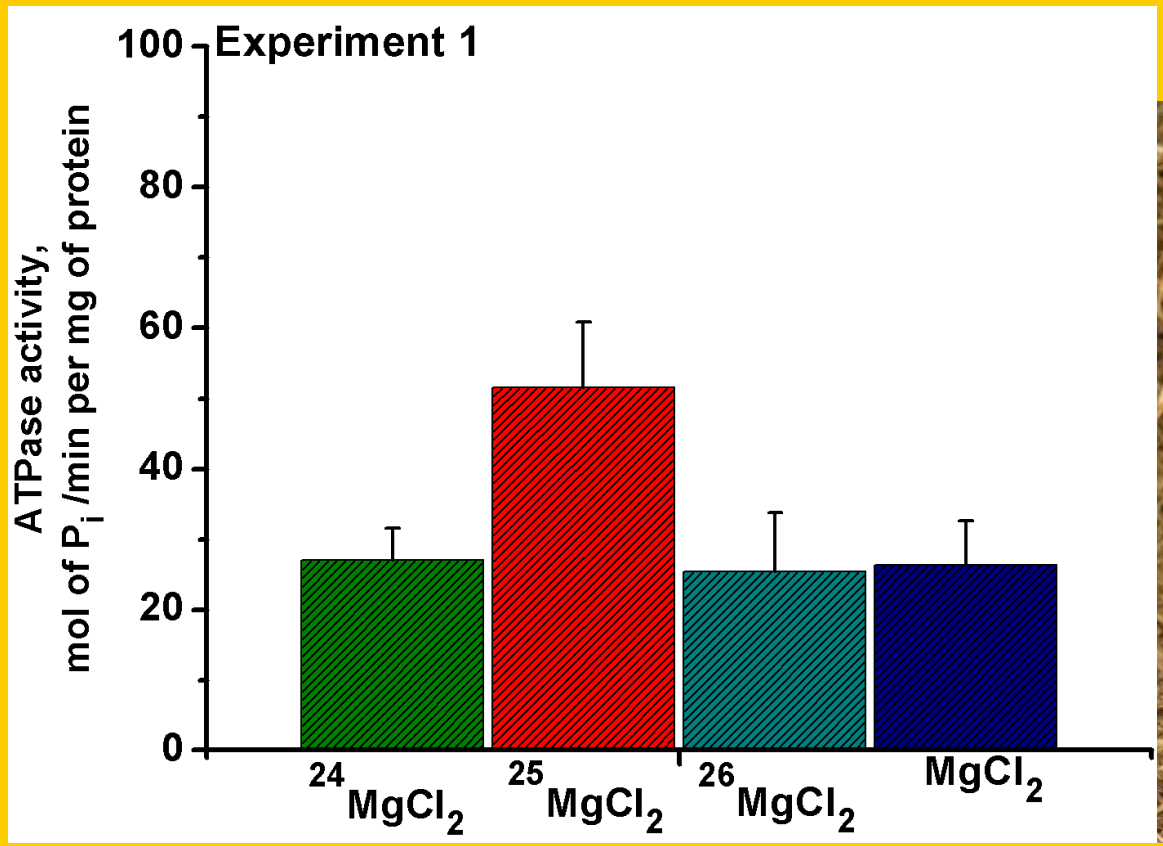
$n = 3, P \leq 0.01$

Effects of $^{25}MgCl_2$ (magnetic isotope, nuclear spin I=5/2), $^{24}MgCl_2$ (nonmagnetic, I=0) and $^{26}MgCl_2$ (nonmagnetic, I=0) on ATP hydrolysis catalyzed by myosin



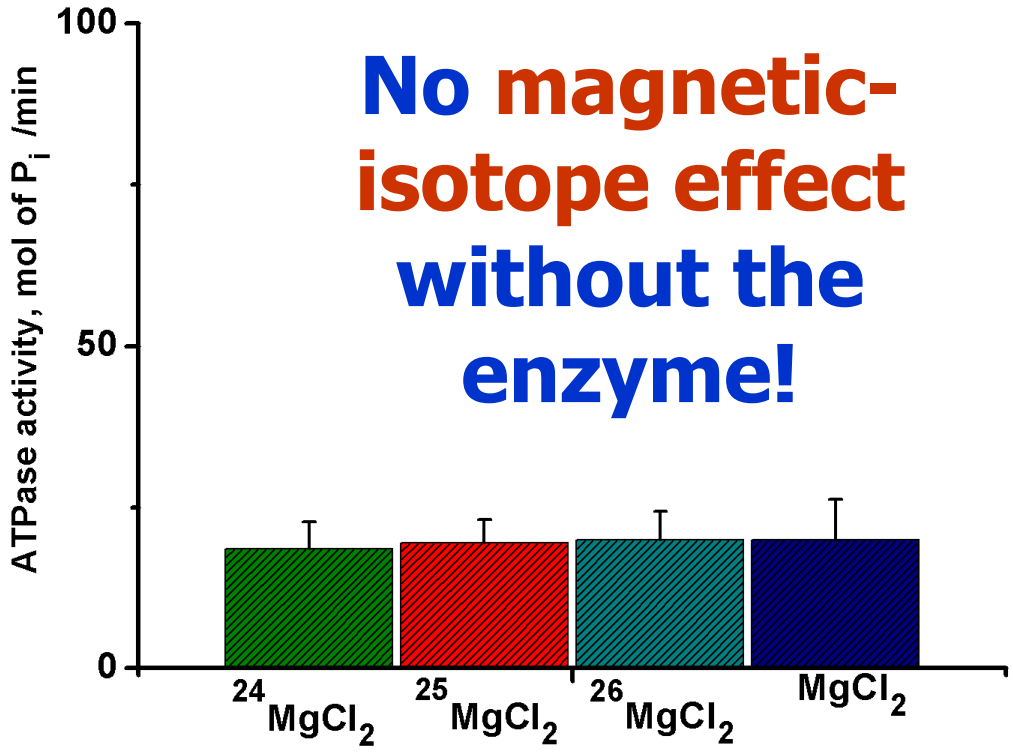
$n = 4, P \leq 0.01$

Effects of $^{25}MgCl_2$ (magnetic isotope, nuclear spin I=5/2), $^{24}MgCl_2$ (nonmagnetic, I=0) and $^{26}MgCl_2$ (nonmagnetic, I=0) on ATP hydrolysis catalyzed by myosin

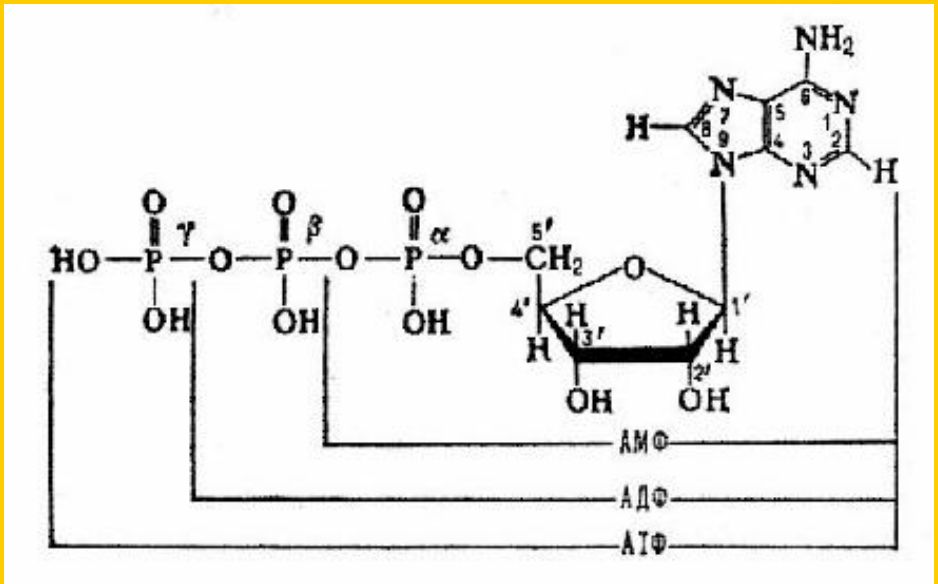


$n = 3, P \leq 0.01$

The rates of spontaneous non-enzymatic ATP hydrolysis in the aqueous solutions supplemented with $^{24}MgCl_2$, $^{25}MgCl_2$, $^{26}MgCl_2$ or "natural" $MgCl_2$ (natural isotope abundance), $m \pm SD$, $n = 3$.



Nuclear Spin Catalysis in Hydrolysis of ATP by Myosin



Energy from ATP (≈ 0.54 eV)

↓^{25}Mg

Energized conformation of macromolecule (a low level triplet state)

↓

Acceleration of ATP hydrolysis

Nuclear Spin Catalysis in Hydrolysis of ATP by Myosin

Energy from ATP (≈0.54 eV)

↓

Energized conformation of macromolecule
(a low level triplet state)

↓

Transfer of electron density onto Mg^{2+} with formation of a virtual ion-radical pair
$[Mg^{+}\ ATP^{\bullet}]^{T}$ or $[Mg^{+}\ OH^{\bullet}]^{T}$ or $[Mg^{+}\ RSH^{\bullet}]^{T}$

↓ ^{25}Mg

Triplet-singlet conversion of the ion-radical pair
$[Mg^{+}\ ATP^{\bullet}]^{T} \rightarrow [Mg^{+}\ ATP^{\bullet}]^{S} \rightarrow [Mg^{2+}\ ATP^{-}]$,
$[Mg^{+}\ OH^{\bullet}]^{T} \rightarrow [Mg^{+}\ OH^{\bullet}]^{S} \rightarrow [Mg^{2+}\ OH^{-}]$, etc.

↓

Acceleration of ATP hydrolysis

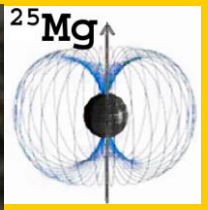
Back to the future - Metchnikoff arises?

Aging is caused by toxic products from intestine microflore (*Elia Mechnikoff, 1907)*

Magne B6 (magnesium lactate + magnesium pidolate + pyridoxine, "Sanofi-Winthrop Industrie"

→ Magne-25 B6

Medical biophysics based on the stable magnetic isotopes?



Step by step, be steady in your purpose! (Mao Tsedun)

Conclusion: **Living cells do perceive the difference between magnetic and non-magnetic nuclei of the same element - perceive the nuclear magnetism.**

Prospect: **stable magnetic isotopes open the novel ways to control over efficiency and reliability of cell nanoreactors.**

Thank you very much for your attention!