Reviews

Nuclear spin catalysis in biochemical physics*

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Magnetic isotope effects have been recently discovered in living nature. They were observed for the first time in experiments on cells enriched with various magnesium isotopes, magnetic ^{25}Mg or non-magnetic ones. A catalytic effect of the magnetic isotope of magnesium was discovered in experiments with myosin, the most important biomolecular motor utilizing the energy of ATP to perform mechanical work. The rate of ATP hydrolysis with the magnetic ^{25}Mg isotope is 2.0—2.5 times higher than that obtained with nonmagnetic ^{24}Mg or ^{26}Mg. A similar effect of the nuclear spin catalysis was experimentally observed for zinc isotopes. The rate of ATP hydrolysis in the case of magnetic ^{67}Zn increased by 40—50% as compared to that observed experimentally for nonmagnetic isotopes (^{64}Zn or ^{68}Zn). Catalytic effects of the magnetic isotope of magnesium were also experimentally found for H^+-ATPase isolated from yeast mitochondria and ATPase of the plasma membrane of the myometrium. The magnetic isotope effect indicates unambiguously that the chemomechanical processes involve a limiting step catalyzed by biomolecular motors, which depends on the electronic spin state, and that this step is accelerated in the presence of nuclear spin of the magnetic isotope.

Key words: spin chemistry, magnetic isotope effect, nuclear spin catalysis, biomolecular motors, enzymes, myosin, ATP.

Introduction

Free radicals and free-radical reactions in living nature, cells, and tissues have been known for a long time.[1—3] Many chemical elements possess two types of their stable isotopes, *viz.*, non-magnetic and magnetic ones.[4] There is the so-called magnetic isotope effect (MIE) known in chemistry. The MIE is experimentally observed as a significant change in the rate and yield of products in a reaction involving free radicals and/or radical ion pairs that depends on whether the starting reagents contain magnetic or non-magnetic isotopes of the same element.[5—10] The MIE is a direct consequence of the law of conservation of angular momentum, the electron angular momentum (spin) in this case. The total spin of reaction products has to be equal to the total spin of the starting reagents. Similar spin forbiddingness arises in physical processes, *e.g.*, dur-

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ing singlet-triplet transitions in molecules and solids.[11] To avoid the restriction dictated by the spin conservation law, it is necessary to change the spin state of reactants. The conversion of spins is maintained by a magnetic field, an external field (Zeeman interaction) or a field of atomic nucleus (Fermi hyperfine interaction of spins of electrons and the nucleus).[5—11]

The works, wherein a question about the existence of MIE ("new isotopy") in biochemistry was brought up for the first time, attracted attention of researchers to this problem.[12,13]

This review summarizes the results of experiments with bacterial and yeast cells enriched with various isotopes of magnesium.[14—20] In these works, MIE has been for the first time discovered in living cells. Results of experiments on the effect of various magnesium and zinc isotopes on myosin, the most important biomolecular motor utilizing the energy of ATP to perform mechanical work, are also presented.[21—23] These works revealed a catalytic effect of the nuclear spin of magnetic isotope on the ATP-hydrolase activity and initiated discussion for possible mechanisms of nuclear spin catalysis in the molecular motors of bioenergetics.

Magnetic isotope effects in living cells

Magnesium is of particular interest as the natural element. The Mg^{2+} ion is a mandatory cofactor for many important enzymes, including those for the synthesis and hydrolysis of ATP, DNA and RNA polymerase, and ribonuclease.[2] Magnesium has three stable naturally occurring isotopes: ^{24}Mg, ^{25}Mg, and ^{26}Mg. The ^{25}Mg isotope is magnetic since it has a nuclear spin ($I = 5/2$), while ^{24}Mg and ^{26}Mg are non-magnetic isotopes ($I = 0$). The natural abundance ratios for ^{24}Mg, ^{25}Mg, and ^{26}Mg isotopes are 78.7, 10.13, and 11.17%, respectively.[4] Consequently, cells and tissues mostly contain non-magnetic isotopes of magnesium, *viz.*, 89.87% or approximately one magnetic isotope among ten non-magnetic ones. However, in order to detect MIE, it is necessary to replace non-magnetic isotopes for a magnetic one of the same element. On this purpose, procedures were developed for growing living cells on a medium enriched with one type of the magnesium isotopes, either magnetic (^{25}Mg) or nonmagnetic (^{24}Mg or ^{26}Mg).[14—20] A high degree of isotopic enrichment (at least 80%) of cells grown in such a medium is achieved naturally, since the content of other magnesium isotope in the growth medium is negligibly low.

Table 1 shows the results of experiments with isotopically enriched cells of *Escherichia coli* (*E. coli*) bacteria.[14,16,19] The growth curve for a bacterial cell culture contains three kinetic sections, *viz.*, a period of relatively slow adaptation to the new growth environment (lag-phase), which goes to a rapid phase of exponential growth (log-phase) and then to a stationary phase. During the stationary phase, cell growth rate declines as substrates, primarily glucose, become exhausted. Two independent series of experiments were carried out, in each of them three samples with an isotope of each type were investigated. One can see from the data listed in Table 1 that cells transferred into a new liquid growth medium adapt continuously this medium significantly faster when it contains the magnetic isotope (^{25}Mg) than in parallel experiments with nonmagnetic isotopes (^{24}Mg or ^{26}Mg). At the same time, there were no differences observed for the nonmagnetic isotopes (^{24}Mg and ^{26}Mg). During the exponential phase, growth rate constants of the cell culture were approximately the same for all the three magnesium isotopes. Furthermore, the MIE was detected during investigations of the activity of antioxidant enzyme, superoxide dismutase (SOD), in cells that had reached the stationary growth phase. The SOD activity in cells grown on a ^{25}Mg-enriched medium was 40% lower than that found for a medium enriched with the nonmagnetic isotope (^{24}Mg). It is known that the level of enzyme activity is determined by the level of its substrate, *viz.*, the level of oxygen radical anions (superoxide radicals, $O_2^{\bullet -}$).[2,24] Apparently, the cells enriched with a magnetic ^{25}Mg not only enter into the stationary phase at a higher rate, but also aging proceeds more readily in this phase as compared to the cells enriched with a nonmagnetic one, due probably to the depletion of nutritional substrates. The metabolism slows down upon aging of cells, and consequently the level of generation of superoxide radicals, as the by-products of oxidative metabolism, decreases too.

The magnetic isotope effect of magnesium was also observed in experiments with another cell model accepted

Table 1. Kinetic parameters for the growth of *E. coli* cells, depending on the type of magnesium isotope in the growth medium. The mean values and the standard deviations ($m \pm SD$) are presented[16,19]

Magnesium isotope	Duration of the adaptation period/h	Constant of growth rate in the exponential phase/h^{-1}
	Experiment I	
$^{24}MgSO_4$	3.0±0.2	1.63±0.02
$^{25}MgSO_4$	2.3±0.3*	1.68±0.05**
$^{26}MgSO_4$	3.4±0.2	1.55±0.06
	Experiment II	
$^{24}MgSO_4$	12.1±0.9	2.0±0.3
$^{25}MgSO_4$	9.8±0.5*	2.3±0.1**
$^{26}MgSO_4$	12.7±0.8	2.1±0.2

* Differences between the mean values for the magnetic and nonmagnetic isotopes are statistically significant ($p \leqslant 0.02$).

** Differences between the mean values for the magnetic and non-magnetic isotopes are statistically insignificant.

commonly, the *Saccharomyces cerevisiae* (*S. cerevisiae*) yeast.[15,17,20] The effect of various magnesium isotopes on the kinetics of postradiation recovery of yeast after their irradiation with X-rays or short-wave UV light was evaluated in those works (Table 2). Average values of kinetic parameters and standard deviation are included in the Table. Experiments under ionizing irradiation were repeated four times for each magnesium isotope and five times for each isotope under UV irradiation. The survival rate for cells transferred to a nutrient medium (agar) immediately after the irradiation did not exceed few percents. After their irradiation, the most of cells do not have enough time to repair the damaged genetic structures before the mitosis, so non-viable daughter cells are formed during cell division. Incubation in a "starving environment", wherein cells are not divided, provides them with some additional time for repair process and consequently, increases the survival rate. It has been found that cells enriched with a magnetic isotope of magnesium are recovered more efficiently than cells enriched with a non-magnetic isotope. The recovery kinetics of ^{25}Mg enriched cells exhibits a significantly higher constant of the recovery rate as compared to the cells enriched with ^{24}Mg. Moreover, the fraction of irreversible damages in cells enriched with the magnetic isotope is by 50—60% lower than that for a non-magnetic isotope.

The magnetic isotope effect was also observed in experiments with UV irradiation. The recovery rate constant was two times that found for the cells enriched with ^{25}Mg than that for ^{24}Mg-enriched cells. However, in contrast to the experiments with ionizing radiation, the fraction of irreversible radiation damages ensued from UV irradiation does not depend practically on the type of isotope selected for the enrichment of cells.

One could assume that the observed differences are caused by non-equal contents of impurities of any foreign elements introduced in the growth medium with different magnesium isotopes. However, the composition of the growth media enriched with various magnesium isotopes was the same according to the elemental analysis data. The elemental composition, including the concentration and isotopic composition of magnesium, was measured by atomic emission spectroscopy and mass spectrometry. The content of impurity elements did not exceed several micromoles per liter, regardless of the type of magnesium isotope. In addition, the impurity elements are presented not only in the preparations of magnesium isotopes, but also in other reagents used for the preparation of a nutrient medium. These elements come into the growth medium in the same amounts, regardless of the magnesium isotope introduced into the same medium, and moreover, in amounts significantly exceeding the concentration of the same impurities introduced with magnesium. Therefore, reliable and significant values of MIE were clearly observed for the magnesium in experiments with isotopically enriched cells of bacteria and yeasts.[14—20]

Table 2. Kinetic parameters for postradiation recovery of *S. cerevisiae* cells enriched with magnesium of the natural isotopic composition or enriched with ^{24}Mg or ^{25}Mg isotopes, after ionizing or UV irradiations[20]

Magnesium isotope	Constant of recovery rate /h^{-1}	Fraction of irreversible damages
Ionizing irradiation (^{60}Co, 300 Gy)		
$MgSO_4$	0.034±0.003	0.75±0.14
$^{24}MgSO_4$	0.029±0.003	0.81±0.15
$^{25}MgSO_4$	0.050±0.004*	0.50±0.17**
UV irradiation (λ = 240—260 nm, 190 J m^{-2})		
$MgSO_4$	0.029±0.002	0.67±0.12
$^{24}MgSO_4$	0.032±0.003	0.70±0.14
$^{25}MgSO_4$	0.058±0.004*	0.61±0.12***

* Differences between the mean values for ^{25}Mg *vs.* ^{24}Mg or Mg are statistically significant ($p = 0.02$).
** Differences between the mean values for ^{25}Mg *vs.* ^{24}Mg or Mg are statistically significant ($p < 0.05$).
*** Differences between the mean values for ^{25}Mg *vs.* ^{24}Mg or Mg are statistically insignificant.

Nuclear spin catalysis in enzymatic reactions: experimental facts

It is known that the Mg^{2+} cation is a required cofactor for the enzymes in the synthesis and hydrolysis of ATP.[2] Accordingly, one may assume that the MIE found in living cells is caused by a higher efficiency of the bioenergetic processes in cells enriched with the magnetic isotope of magnesium. Myosin, the muscle protein, is one among the most explored molecular motors in bioenergetics. The enzyme hydrolyzes a terminal phosphate bond in the ATP molecule to give ADP and inorganic phosphate (P_i), while the energy is released (about 0.54 eV under physiological conditions) to be used for muscle contraction.[2]

In our works, we have evaluated the effect of various magnesium isotopes on subfragment-1 of myosin isolated from smooth muscle (myometrium) of pigs.[21—23] Subfragment-1 of myosin is considered as a sufficient functional unit of myosin, since it retains all its native properties, *viz.*, the catalytic ATP hydrolase activity and the ability to interact with actin. The enzyme activity was estimated according to the Fiske—Subbarow method based on measuring the concentration of colored complex of ammonium molybdate with phosphate P_i, which is produced in the reaction of ATP hydrolysis.

Three independent series of experiments were performed for different myosin preparations isolated at different times from three different animals. Experiments for the each of these preparations were repeated from three to eight times with the each magnesium isotope under the

standard experimental conditions at 37 °C. The reaction medium contained Tris—HCl (20 m*M*, pH 7.2), $CaCl_2$ (0.01 m*M*), KCl (100 m*M*), ATP (3 m*M*), myosin subfragment-1 (20 μg of protein mL^{-1}), and corresponding magnesium chloride (5 m*M*, *i.e.* physiological concentration): $^{24}MgCl_2$, $^{25}MgCl_2$, $^{26}MgCl_2$, or $MgCl_2$ of the natural isotopic composition.[21—23] Figure 1 shows typical results of the experiments performed. Regardless of variability of the mean values of ATPase activity in experimental series, the same MIE was observed in all the series. In the presence of the magnetic isotope, the enzyme activity was 2—2.5 times higher than that for the same enzyme and a non-magnetic isotope. It is important to highlight that the rate of ATP hydrolysis in different experiments with $^{24}MgCl_2$, $^{25}MgCl_2$, $^{26}MgCl_2$, and $MgCl_2$ of natural isotopic composition was the same during the spontaneous hydrolysis of ATP in a reaction media of the same composition containing all the components, except for the enzyme. Thus, the MIE is observed only during the enzymatic hydrolysis of ATP.

Consider next the effects of various zinc isotopes on the ATP-hydrolase activity of subfragment-1 of myosin. Zinc possess five stable isotopes, ^{64}Zn, ^{66}Zn, ^{67}Zn, ^{68}Zn, and ^{70}Zn, whose relative abundances are 48.6, 27.9, 4.1, 18.8, and 0.6%, respectively, wherein ^{67}Zn is magnetic ($I = 5/2$), and the other four isotopes are nonmagnetic ($I = 0$).[4] A standard reaction medium was used, *i.e.*, the same as in experiments with magnesium isotopes, but containing zinc chloride instead of magnesium chloride, *viz.*, 5 m*M* $^{67}ZnCl_2$, $^{64}ZnCl_2$, or $^{68}ZnCl_2$. Two independent series of experiments were performed for enzyme preparations isolated from two different animals; experiments with the each zinc isotope were repeated at least three times for the each enzyme preparation (Fig. 2). It is known that the Zn^{2+} ion is less efficient as a cofactor of myosin than Mg^{2+}. Indeed, the enzyme activity in the presence of non-magnetic zinc ions is lower than that observed in the presence of magnesium ions. However, the rate of ATP hydrolysis in the presence of magnetic zinc isotope (^{67}Zn) was 50—70% higher than that found for nonmagnetic isotopes.

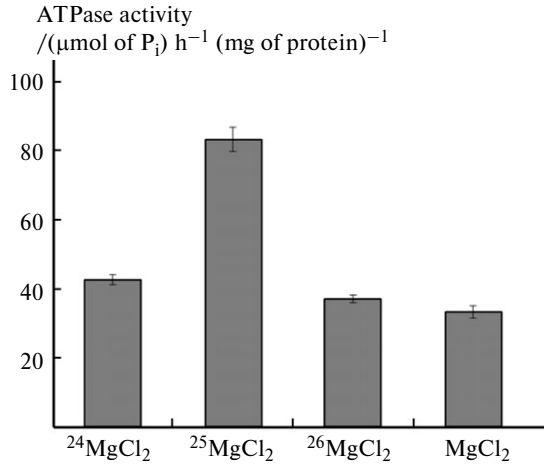

Fig. 1. ATPase activity of myosin subfragment-1 (m±SD) in reaction media containing various magnesium isotopes. Differences between the average values in the experiments for the magnetic isotope (^{25}Mg) and nonmagnetic isotopes of magnesium or magnesium of the natural isotopic composition are statistically significant ($p < 0.01$) (based on data in Ref. 23).

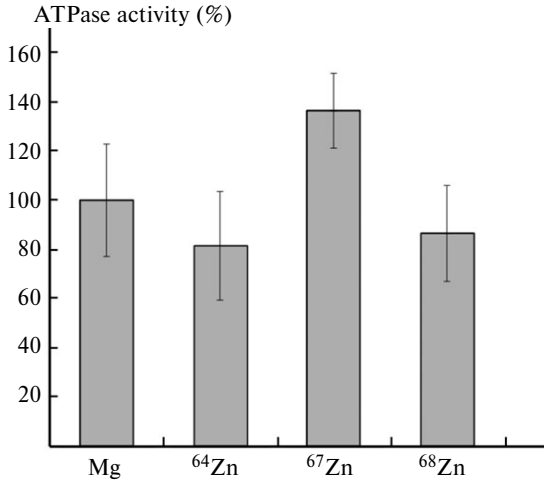

Fig. 2. ATPase activity of myosin subfragment-1 in reaction media containing various zinc isotopes. The data (m±SD) are presented as a percentage of enzymatic activity in the presence of $MgCl_2$ (5 m*M*) of the natural isotopic composition, taken as 100%. Differences between the average values in the experiments for the magnetic isotope (^{67}Zn) and nonmagnetic isotopes of zinc are statistically significant ($p < 0.05$) (based on data in Ref. 23).

Thus, the effect of accelerating the enzymatic hydrolysis of ATP was also found in experiments with zinc isotopes, similarly to the MIE in experiments with magnesium isotopes. The myosin-catalyzed enzymatic hydrolysis of ATP is accelerated by the nuclear spin of magnetic isotope.

A similar catalytic effect of ^{25}Mg nuclear spin was small (20—30%), but statistically significant in the experiments performed with various magnesium isotopes on ATP hydrolysis catalyzed by Mg-dependent ATPase of plasma membranes of myocytes[23] and in experiments with H^+-ATPase (complex MF_0F_1) isolated from yeast mitochondria and incorporated into liposomes.[25]

However, attempts to detect a MIE in experiments aimed at investigating the effect of various magnesium isotopes on the ATP-dependent reaction catalyzed by luciferase were unsuccessful.[26] Luciferase catalyzes the oxidation of luciferin by molecular oxygen in the presence of Mg-ATP complex. The reaction proceeds in two steps. At the first step, luciferase hydrolyzes ATP not to ADP and phosphate, as done by myosin or mitochondrial H^+-ATPase, but to adenosine monophosphate and pyrophosphate. In this case, adenylation of luciferin occurs using the energy of hydrolysis to give luciferyl adenylate. At the second step,

luciferyl adenylate is oxidized by atmospheric oxygen, being converted into the final reaction product, oxyluciferin. Oxyluciferin is formed in an electronically excited state, and its transition to the ground state is accompanied by the emission of a quantum of light in the visible region of the spectrum. The luminescence intensity is proportional to the ATP concentration and serves as a measure of the ATP content in the reaction mixture. Investigations of the luminescence spectra and enzymatic activity of firefly luciferase in the presence of various magnesium isotopes revealed that the kinetics of the luciferin oxidation catalyzed by luciferase and the luminescence spectra do not depend on the type of magnesium isotope.[26] This result is also of practical importance. Currently, the luciferin-luciferase method is the most sensitive quantitative method for the determination of ATP content in biological systems. Since MIE was not detected in the luciferase reaction, this method can be further employed to detect and estimate MIE in ATP-dependent enzymatic reactions, including the synthesis and hydrolysis of ATP.

The MIE was also not observed in experiments with creatine phosphokinase.[27] In the strict sense, creatine phosphokinase is not an enzyme for the synthesis nor hydrolysis of ATP. Creatine phosphokinase (also defined as creatine kinase) catalyzes either the transfer of high-energy phosphate group (~P_i) from the creatine phosphate molecule to ADP to produce ATP or the reverse reaction of ~P_i transfer from ADP to creatine to form creatine phosphate as an "energy depot" of muscle fiber. In this case, the high-energy phosphate bond is neither broken nor formed *de novo*.[2]

Nuclear spin catalysis in enzymatic reactions: discussion of experimental results

A conclusion suggests itself that nuclear spin catalysis is observed only in the work of those enzymes that perform the function of biomolecular motor, *i.e.*, utilize the chemical energy of ATP to perform mechanical work either completely as myosin or at least partially as mitochondrial H^+-ATPase and Mg-dependent ATPase of plasma membranes. In chemistry and physics, the MIE unambiguously indicates that there is a limiting step in a considered process, which depends on the electronic spin state, and that the magnetic field of atomic nucleus (the nuclear spin) promotes this step. In chemistry, the MIE is usually explained by assumption that radical or ion-radical pair exists as an intermediate product of the reaction.[5—10] However, it is known that the reaction of ATP hydrolysis yielding ADP and P_i proceeds according to an acid-base mechanism;[2] therefore, the formation of a radical-ion pair as the reaction intermediate is unlikely. Indeed, MIE is not observed in the non-enzymatic hydrolysis of ATP.

However, the situation is different in the case of ATP hydrolysis catalyzed by a molecular motor. It has been experimentally proven that the ATP hydrolysis initiates electronic-conformational interactions in the active site of enzyme. The energy released from the hydrolysis of ATP causes conformational excitation, *i.e.*, the deformation of the macromolecule.[28,29] In the case of myosin-catalyzed hydrolysis of ATP, the cycle of generation of mechanical stress in the macromolecule consists of several steps, according to quantum mechanical calculations.[30] At the first step, γ-phosphate of ATP is stabilized in the form of dissociated metaphosphate ($P_\gamma O^{3-}$), while the products of hydrolysis of ADP and P_i remain in the active center of enzyme in close contact and their release requires myosin binding to actin filaments. This is consistent with the well-known fact of reversibility of the myosin-catalyzed ATP hydrolysis reaction. As long as the hydrolysis products, ADP and P_i, remain bound by myosin and in close contact, they can form ATP again.[30]

It can be assumed that under the conditions of electron-conformational excitation of macromolecule, electron density is transferred inside the active center of enzyme to ADP or Mg^{2+}, *e.g.*, from the OH^- group of the bound water molecule or from the NH_2 group of Glu-459 to yield the corresponding radical ion pair. After that, the ADP oxyanion nucleophilically attack the inorganic phosphate to give ATP. A stable spin state of the product, Mg-ATP (Zn-ATP in experiments with Zn), has to be singlet (electron spin $S = 0$). The nuclear spin of ^{25}Mg (or ^{67}Zn) is able *via* the hyperfine interaction with the unpaired electron of radical-ion pair to convert this pair bound by myosin into a triplet state ($S = 1$). By developing the spin forbiddance, the nuclear spin of ^{25}Mg (or ^{67}Zn) isotope hinders the undesirable reverse reaction of ATP synthesis, thus facilitating the direct reaction of ATP hydrolysis. A hypothesis about the key role of virtual radical ion pair in the synthesis of ATP *via* oxidative phosphorylation has been proposed about 50 years ago.[31]

An alternative explanation for the nuclear spin catalysis in the reactions of ATP hydrolysis catalyzed by molecular motors may be offered.[32] The energy released from the hydrolysis of ATP (~0.54 eV) is not high enough for the electron-conformational transition of macromolecule to the singlet excited state. However, this energy is sufficient for a transition to the lower triplet state ($S = 1$), but such a transition from the ground state ($S = 0$) is prohibited by the spin conservation law. The presence of magnetic isotope (^{25}Mg or ^{67}Zn) changes the situation: the nuclear spin of this isotope removes the spin forbiddance. Therefore, the magnetic isotope (^{25}Mg or ^{67}Zn) accelerates the chemomechanical cycle in the enzymatic reaction, providing the necessary spin conversion of electronic-conformational state of the macromolecule to the triplet state (coherent bosons).[32] Therefore, the hypothesis of excited solitons in one-dimensional molecular systems and solitons in protein molecules is of certain interest as the basis of the molecular mechanism of muscle contraction.[33]

Now we can consider another possible explanation for the catalytic effect of nuclear spin of ^{25}Mg (and ^{67}Zn). The ATP hydrolysis catalyzed by the molecular motor is accompanied by a significant conformational rearrangement in the macromolecule. In this case, processes of dehydration and rehydration of the electrically charged amino acid groups occur. Meanwhile, there are two isomers of water molecule, which differ in the mutual alignment of nuclear spins of hydrogen, *viz.*, *ortho*-H_2O with parallel orientation and *para*-H_2O with antiparallel orientation of the proton spins. At room temperature, *ortho*-H_2O accounts for 75% of the total volume, according to quantum statistics.[34] It can be assumed that *ortho*-H_2O molecules exhibit a preferred affinity towards L-amino acids, as compared to *para*-H_2O ones.[35] In this case, the movement during the conformational transformation of the macromolecule is hindered for predominantly bound *ortho*-H_2O molecules, while the spin-rotational interactions of protons are too weak for maintaining the proper efficiency of *ortho—para* transitions. Obviously, the magnetic ^{25}Mg (or ^{67}Zn) isotope can significantly improve such a situation, *viz.*, eliminating the problem of spin exclusion, thus ensuring the required conversion rate of water isomers.

In the molecular motors operating on a non-magnetic isotope of magnesium, the spin catalysis can be theoretically performed by the nuclear spins of hydrogen (^1H, $I = 1/2$) and phosphorus (^{31}P, $I = 1/2$). A relatively high catalytic activity of the magnetic isotopes of magnesium and zinc is apparently due to nuclear spins of ^{25}Mg ($I = 5/2$) and ^{67}Zn ($I = 5/2$) that are five times those of ^1H and ^{31}P and consequently, they generate stronger local magnetic fields (hyperfine interaction constant ~21 mT) in the active center of the enzyme.

Conclusions

The cells of *E. coli* bacteria are more quickly adapted to a growth medium enriched with the magnetic isotope of magnesium (^{25}Mg), as compared to the cells transferred in a medium with the nonmagnetic isotope (^{24}Mg or ^{26}Mg). Experiments with the cells of *S. cerevisiae* yeast revealed the radioprotective effect of the magnetic magnesium isotope. Cells enriched with the magnetic isotope of magnesium are recovered faster than those enriched with a non-magnetic isotope after their irradiation with ionizing radiation or short-wave UV light. Living cells perceive the nuclear magnetism. Moreover, the MIE have been observed in experiments with myosin. The rate of enzymatic hydrolysis of ATP in the reaction medium with the magnetic isotope of magnesium is twice that for the non-magnetic isotopes of magnesium. A similar effect, the nuclear spin catalysis, was found in experiments with zinc isotopes used as a cofactor for enzymatic hydrolysis of ATP. Detailed mechanisms of MIE in living cells and enzymatic reactions are the tasks for further investigations.

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The author declares no competing interests.

References

1. B. Commoner, J. Townsend, G. E. Pake, *Nature*, 1954, **174**, 689.
2. D. L. Nelson, M. M. Cox, *Lehninger Principles of Biochemistry*, Freeman, New York, 2008, 520 pp.
3. V. K. Koltover, *Russ. Chem. Bull.*, 2010, **59**, 37; DOI: 10.1007/s11172-010-0042-2.
4. *Encyclopedia of Nuclear Magnetic Resonance*, Eds D. M. Grant, R. K. Harris, Wiley, Chichester, 1996.
5. A. L. Buchachenko, R. Z. Sagdeyev, K. M. Salikhov, *Magnitnye i spinovye effekty v khimicheskikh reaktsiyakh* [*Magnetic and Spin Effects in Chemical Reactions*], Nauka, Novosibirsk, 1978, p. 337 (in Russian).
6. N. J. Turro, B. Kraeutler, *Acc. Chem. Res.*, 1980, **13**, 369.
7. Y. B. Zeldovich, A. L. Buchachenko, E. L. Frankevich, *Sov. Phys. Uspekhi*, 1988, **155**, 3.
8. B. Brocklenhurst, *Chem. Soc. Rev.*, 2002, **31**, 301.
9. A. L. Buchachenko, R. G. Lawler, *Acc. Chem. Res.*, 2017, **50**, 877.
10. A. L. Buchachenko, *Phys. Usp.*, 2019, **189**, 47.
11. V. V. Kveder, Yu. A. Osipiyan, A. I. Shalynin, *Sov. Phys. JETP*, 1982, **56**, 389.
12. A. L. Buchachenko, *Magnetic Isotope Effect in Chemistry and Biochemistry*, Nova Science Publ., New York, 2009.
13. A. L. Buchachenko, D. A. Kouznetsov, N. N. Breslavskaya, *Chem. Rev.*, 2012, **112**, 2042.
14. T. N. Bogatyrenko, Ye. A. Kudryashova, L. V. Tumanova, V. K. Koltover, *Tez. dokl. V Mezhdunar. kongressa "Slabye i sverkhslabye polya i izluchenia v biologii i meditsine"* [*Proc. V Int. Congress "Weak and superweak fields and radiation in biology and medicine"*], St. Petersburg, 2009, p. 92 (in Russian).
15. D. M. Grodzinsky, T. A. Evstyukhina, V. K. Koltover, V. G. Korolev, Y. A. Kutlakhmedov, *Reports Natl. Acad. Sci. Ukraine*, 2011, **12**, 153.
16. V. K. Koltover, U. G. Shevchenko, L. V. Avdeeva, E. A. Royba, V. L. Berdinsky, E. A. Kudryashova, *Dokl. Biochem. Biophys.*, 2012, **442**, 12.
17. V. K. Koltover, V. G. Korolev, Y. A. Kutlakhmedov, in *Ionizing Radiation: Applications, Sources and Biological Effects*, Eds E. Belotserkovsky, Z. Ostaltsov, Nova Science Publ., New York, 2013, p. 117.
18. V. K. Koltover, *Russ. Chem. Bull.*, 2014, **63**, 1029.
19. L. V. Avdeeva, V. K. Koltover, *Moscow Univ. Chem. Bull.*, 2016, **71**, 160.
20. L. V. Avdeeva, T. A. Evstyukhina, V. K. Koltover, V. G. Korolev, Yu. A. Kutlakhmedov, *Nucl. Phys. At. Energy*, 2019, **20**, 271.

21. V. K. Koltover, R. D. Labyntseva, V. K. Karandashev, S. O. Kosterin, *Biophysics* (*Engl. Transl.*), 2016, **61**, 200.
22. V. K. Koltover, R. D. Labyntseva, S. O. Kosterin, in: *Myosin: Biosynthesis, Classes and Function*, Ed. D. Broadbent, Nova Science Publ., New York, 2018, p. 135.
23. V. K. Koltover, R. D. Labyntseva, V. K. Karandashev, *Biophysics* (*Engl. Transl.*), 2020, **65**, 416.
24. R. A. Guskova, M. M. Vilenchik, V. K. Koltover, *Biophysics* (*Engl. Transl.*), 1980, **25**, 102.
25. V. K. Koltover, P. Graber, V. K. Karandashev, I. Starke, P. Turina, in: *Abstracts of 11th Int. Conf. "Biocatalysis: Fundamentals and Applications"*, Innovations and High Technologies MSU Ltd, Moscow, 2017, p. 50.
26. D. V. Smirnova, V. K. Koltover, S. V. Nosenko, I. A. Strizhova, N. N. Ugarova, *Moscow Univ. Chem. Bull.*, 2018, **73**, 158.
27. D. Crotty, G. Silkstone, S. Poddar, R. Ranson, A. Prina-Mello, M. T. Wilson, J. M. D. Coey, *Proc. Natl. Acad. Sci. USA*, 2019, **109**, 1437.
28. M. V. Volkenstein, *General Biophysics*, Acad. Press, New York, 1983.
29. D. S. Chernavskiy, N. M. Chernavskaya, *"Belok-mashina". Biologicheskie makromolekulyarnye konstruktsii* [*"Protein as a machine". Biological macromolecular constructs*], Yanus-K, Moscow, 1999 (in Russian).
30. F. A. Kiani, S. Fischer, *Proc. Natl. Acad. Sci. USA*, 2014, **111**, 2947.
31. L. A. Blumenfeld, V. K. Koltover, *Mol. Biol.* (*Engl. Transl.*), 1972, **6**, 130.
32. V. K. Koltover, *J. Mol. Liquids*, 2017, **235**, 44.
33. A. S. Davydov, *Sov. Phys. Uspekhi*, 1982, **25**, 898.
34. V. I. Tikhonov, A. A. Volkov, *Science*, 2001, **296**, 2363.
35. Y. Scolnik, I. Portnaya, U. Cogan, S. Tal, R. Haimovitz, M. Fridkin, A. C. Elitzur, D. W. Deamer, M. Shinitzky, *Phys. Chem. Chem. Phys.*, 2006, **8**, 333.

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