Reliability in Nanoengineering: Nuclear Spin of Magnesium-25 as Reliability Factor in Molecular and Biomolecular Nanoreactors

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ABSTRACT

The trend of nanoscaling brings engineering down to the dimensions of molecular structures. At the same time, it poses the problem of how to create reliable systems from molecular components which experience permanent thermal, mechanical and environmental fluctuations. The main line of creating reliable devices from unreliable components in living systems is preventive maintenance of functional components, first and foremost, prophylaxis of failures. The nuclear spin magnetic moment of magnesium-25 affords such a prophylactic effect in living cells. We have found that cells of *Escherichia coli* grow much faster on the medium containing magnetic isotope ^{25}Mg than on the media containing nonmagnetic ^{24}Mg or ^{26}Mg. Furthermore, there is the evidence that the cells on ^{25}Mg produce less superoxide free radicals as the faulty by-products of metabolism by comparison with the cells on nonmagnetic isotopes. In essence, the nuclear magnetic field of ^{25}Mg prevents the free-radical failures in the biomolecular nanoreactors. The preventive antioxidant effect of ^{25}Mg opens the ways toward novel medicine based on this magnetic isotope, including anti-aging drugs and radio-protectors. On the same nuclear spin-catalysis background, magnetic isotopes hold considerable promise for the magnetic-field control in nanoengineering and nanomedicine.

Keywords: nanotechnology, nanoengineering, reliability, nanoreactors, magnetic isotopes

INTRODUCTION

Nanotechnology – a catchall term for engineering materials sized between 1 and 100 billionths of a meter – is widely seen as having enormous scientific and commercial potential. The idea that engineering can be extended towards the molecular scale, to electronic devices of high efficiency based on single molecules and so on, has become currency over the past decade. This trend of nanoscaling brings engineering down to the dimensions of molecular structures. At the same time, it brings technical devices down to intrinsic instability of functional parameters due to thermal, mechanic and other fluctuations. That raises the question as to whether operation of the nanoscaling devices can be reliable. One can lower temperature up to helium values at which thermal fluctuations are less. The alternative way is to follow the general theory of reliability and bionics [1]. Insertion of redundant amount of the functional nanocomponents, which fulfill one and the same function, magnifies the system reliability. Another line of creating the highly reliable systems from unreliable components is preventive maintenance or prophylaxis of failures [2]. Keeping in mind the possible free-radical damages, researchers who fabricate new composite materials embedded with organic dye molecules and paramagnetic metal atoms should provide the composites with appropriate antioxidants as well. Along this nanoengineering line the general principles of spin-chemistry, amongst them – control of chemical reactivity by selective isotope modification, hold considerable promise for basic research as well as for creating reliable optoelectronic and nanophotonic devices.

1 NUCLEAR SPIN CATALYSIS IN MOLECULAR NANOREACTORS

Apart from energy control (the law of conservation of energy), any chemical reaction as electron-nuclear rearrangement of reactants into products is controlled by angular momentum, spin, of reactants. The total spin of products must be identical to that of reactants. This law of spin conservation immediately follows from quantum mechanics, from the fundamental and universal Pauli principle: no two electrons may occupy the same quantum state simultaneously (see, for example, [3, 4] and references therein). Correspondingly, acceleration of the free-radical reactions can be achieved through changes in the total electron spin of reactants by interaction with magnetic fields of magnetic nuclei. This is known as magnetic isotope effect, a new trend in chemical physics within recent years [5]. The discovery of the magnetic isotope effects of magnesium-25 in biochemical reactions has become another breakthrough of great importance [6].

A pair of free radicals, each with electron spin $S = 1/2$, can form a chemical bond ($S = 0$) if the spin state of the pair is singlet, i.e. spins of the two electrons are subtracted to give the net $S = 0$ (spin multiplicity is one). If the spin state of the radical pair is triplet, i.e. the spins of two electrons are added up to give the net $S = 1$ (spin multiplicity is three), then the radicals cannot react immediately. It means that only one-quarter of encounters, when the radical pair is in the singlet state, gives the recombination product while three-quarters of the initial radical pairs are inhibited from

the reaction. To lift the ban on the reactions forced by the law of spin conservation, spins of the reactants must be changed. Magnetic fields are the only means that are able to change the spin states. Accordingly, the probability of chemical reaction is a function of parameters of these interactions:

$$P = f(H;\ \omega;\ H_1;\ J;\ a;\ I;\ m_I;\ \mu_n) \qquad (1)$$

where H is applied magnetic field (Zeeman interaction that produces magnetic field effect); ω and H_1 are frequency and amplitude of microwaves (the interaction that produces chemically detected magnetic resonance and stimulated nuclear polarization); J is exchange energy (the exchange interaction). For example, the reactions of organic free radicals or ion-radicals can be catalyzed via interaction of partners of the radical pair with a foreign, third spin carrier, like nitroxide radical, that produces 'electron spin catalysis' [4]. The equation also contains parameters of hyperfine coupling a, nuclear spin I, nuclear spin projection m_I, and nuclear magnetic moment μ_n, i.e. the parameters of interactions of electron spins with magnetic nuclei (Fermi coupling) responsible for chemically induced dynamic nuclear polarization, microwave emission (chemical maser) and magnetic isotope effect.

The magnetic isotope effect (MIE) is a purely kinetic phenomenon and manifests itself as the dependence of the reaction rate on the nuclear spins of the reactants. Namely, the reaction will show different reaction rates and different yields of products according to whether the reagents contain magnetic or nonmagnetic isotopes. In molecular liquids, MIE has been discovered for a number of magnetic isotopes, among them H–D, ^{13}C, ^{17}O, ^{29}Si, ^{33}S, ^{73}Ge, ^{117,119}Sn, ^{199,201}Hg, and ^{235}U [5]. MIE selects isotopes by spin and magnetic moment while classical isotope mass effect (CIE) selects isotopic nuclei in accordance with their masses. For example, it has been recently found that the photochemical reduction of Hg-compounds by natural sunlight in aquatic ecosystems leads to both mass-dependent fractionation of Hg isotopes, due to the CIE, and mass-independent fractionation of the odd-mass Hg isotopes, due to the MIE [7].

2 NUCLEAR SPIN CATALYSIS IN BIOMOLECULAR NANOREACTORS

By analogy with electron spin catalysis, the enhancement of the reaction rate by the nuclear spins of the reactants can be denoted as the 'nuclear spin catalysis' [8, 9]. Recently, this phenomenon has been discovered for magnetic isotope of magnesium, ^{25}Mg, in biomolecular nanoreactors of living cells [8–11].

Energetic demands of every operation in living systems are met by molecules of adenosine triphosphate (ATP). Most of ATP is produced by specific biomolecular nanoreactors, the enzymes organized in respiratory electron transport chains (ETCs) [12]. Normal function of the ETC's enzymes, be it mitochondrial nanoreactors in eukaryotic cells of animals or similar nanoreactors of bacteria cells, is in the transport of electrons, one by one, from the electron donor molecules to the end enzyme, cytochrome oxidase, from which the electrons are transferred to molecules of oxygen with two-electron reduction of oxygen into water. Free energy released during the electron transport is used for synthesis of ATP from adenosine 5'-diphosphate (ADP) and inorganic phosphate (P_i), the so-called "oxidative phosphorylation [12].

Synthesis of ATP depends on the ion of Mg^{2+} as the obligatory cofactor. Among three stable magnesium isotopes, ^{24}Mg, ^{25}Mg and ^{26}Mg with natural abundance 78.7, 10.1 and 11.2% respectively, only ^{25}Mg has the nuclear spin (I = 5/2) and, therefore, has the magnetic moment. Two other stable isotopes, ^{24}Mg and ^{26}Mg, are spinless (I = 0) and, therefore, have no magnetic moment. In experiments with isolated mitochondria, it has been discovered that the rate of synthesis of ATP with the magnetic nucleus ^{25}Mg was essentially higher than that with the spinless nonmagnetic nuclei ^{24}Mg or ^{26}Mg, while there was no difference between the effects of $^{24}Mg^{2+}$ and $^{26}Mg^{2+}$ on the ATP synthesis [6].

Furthermore, magnetic isotope effects of ^{25}Mg have been discovered in our experiments with bacteria *Escherichia coli*. We have revealed that the cells, which grow on the medium containing magnetic ^{25}Mg ($^{25}MgSO_4$), multiply essentially faster than the cells, which grow in the media containing nonmagnetic isotopes of magnesium. Moreover, the cells grown on the magnetic isotope of magnesium have demonstrated twice as much the ability to form colonies (CFU) than the cell grown on the nonmagnetic isotopes of magnesium [10]. In addition, it has been found that the cells, that grow on ^{25}Mg exhibit significantly less activity of superoxide dismutase (SOD), by 40 per cent, when compared to the cells grown on nonmagnetic ^{24}Mg [11]. SOD is the enzyme that eliminates superoxide radicals ($O_2^{\bullet -}$), the faulty by-products of the electron-transport nanoreactors of oxidative phosphorylation. Activity of this specialized enzyme is adjusted to the intracellular level of the $O_2^{\bullet -}$ radicals (see, for example, [12]). Hence, the lower level of SOD activity testifies the lower production of $O_2^{\bullet -}$ in the case when the cells are supplied with the magnetic isotope.

It is generally known that the $O_2^{\bullet -}$ radicals can initiate chemically reactive oxygen species that produce oxidative damages in cells and tissues. It means that nuclear spin of ^{25}Mg actually exerts the preventive antioxidant effect. This preventive antioxidant effect of the nuclear spin, that ^{25}Mg favors the less production of reactive oxygen species, should obviously prolong lifetimes of the electron-transport nanoreactors. Therefore, it can reveal itself as the kinetic nuclear-spin selection of the favorable magnetic ^{25}Mg, the kinetic isotope enrichment, in the processes of recycling and regeneration of the electron-transport nanoreactors in nature. For example, one can expect for the favorable magnetic isotope, ^{25}Mg, selection in recycling and

regeneration of mitochondria in cells and tissues with aging of animals.

Contrary, in the case of photosynthetic nanoreactors, one can predict undesirable pro-oxidant effect of the magnetic ^{25}Mg nucleus. Indeed, it is known that the function of the vast majority of chlorophyll molecules (Chl) as the derivatives of the magnesium-protoporphyrin complexes is to absorb light energy and transfer it to the specific energy sinks, the so-called reaction centers of the photosynthetic nanoreactors [12]. While performing this energy-transfer function, the light-exited Chl molecules are in the singlet state (^{1}Chl*, electron spin S = 0). However, there is probability of the radiationless relaxation into the triplet state (^{3}Chl, S = 1) followed by formation of singlet oxygen, $^1O_2$, the molecules of which are substantially more reactive by comparison with the usual triplet O_2 molecules and, thereafter, produce oxidative damages. As nuclear spin of ^{25}Mg can catalyze the conversion of ^{1}Chl* into the triplet ^{3}Chl, one can expect for the higher yield of $^1O_2$ and, thereafter, more photodynamic damages when chlorophyll molecules contain ^{25}Mg instead of the spinless ^{24}Mg or ^{26}Mg [8, 9]. Correspondingly, it is beyond reason to hope for selection of the magnetic isotope, ^{25}Mg, in the case of algae or green plants. In addition, the functional disadvantage of ^{25}Mg can be followed by increased synthesis of carotenoids and other natural antioxidants. Indeed, measurements of magnesium isotopic composition of the chlorophylls extracted from cyanobacteria and similar analysis of the chlorophyll forms in the leaves of English Ivy (*Hedera helix* L.) have revealed the isotope distribution following usual classical mass-isotope effect with no evidence for the depletion of ^{25}Mg [13].

Apart from magnesium, there are many other elements which have both kinds of stable isotopes, nonmagnetic and magnetic ones including carbon (^{12}C, I = 0 vs. ^{13}C, I = 1/2), oxygen (^{16}O, I = 0 vs. ^{17}O, I = 5/2), silicon ($^{28, 30}$Si, I = 0 vs. ^{29}Si, I = 1/2), calcium ($^{40, 42, 44, 48}$Ca, I = 0 vs. ^{43}Ca, I = 7/2), iron ($^{54, 56, 58}$Fe, I = 0 vs. ^{57}Fe, I = 1/2), zinc ($^{64, 66, 68}$Zn, I = 0 vs. ^{67}Zn, I = 5/2), etc. [14]. For example, nuclear spin of ^{17}O should lift the spin ban over the reaction of the mitochondrial ubisemiquinone radicals with oxygen, thereby catalyzing formation of $O_2^{\bullet-}$. As a result, one can expect for more reactive oxygen radicals and more free-radical damages due to ^{17}O in comparison with nonmagnetic ^{16}O and ^{18}O. The pro-oxidant action of ^{17}O can reveal itself as selective enrichment of free-radical peroxidation products with this unfavorable magnetic isotope as compared with ordinary metabolites. However, up to date, there have been no efforts to detect magnetic isotope effects for other elements, except magnesium, in biopolymer nanoreactors.

CONCLUSIONS AND OUTLOOK

The magnetic isotope effect ('nuclear spin catalysis'), as such, always and unambiguously indicates that the reaction under study is spin-selective process with participation of paramagnetic intermediates, such as a free radical pair, an ion-radical pair or a triplet state that undergo the spin conversion. Hence, the finding of MIE indicates that there is a spin-selective 'bottleneck' of the process under investigation. The preventive antioxidant effect of ^{25}Mg opens the ways toward novel medicine based on this magnetic isotope including anti-aging drugs, and radio-protectors. On the same nuclear spin-catalysis background, magnetic isotopes hold considerable promise for the magnetic-field control over efficiency and reliability of nanoreactors in nanoengineering and nanomedicine.

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