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A Study of Single Domain Magnetic Nanoparticles Towards Reactions by Low Frequency Magnetic Fields

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Abstract : The dynamics of single domain magnetic nanoparticles cross-linked into multi-particle aggregates by organic ligands is considered. Mechanical factors of the effect of low frequency magnetic field on macro molecules attached to magnetic nanoparticles/aggregates within a suspension or gel are analyzed. The optimum conditions ensuring the best control over biochemical reactions in suspension by an external magnetic field (i.e., the ranges of frequency and magnetic field intensities, and the size of magnetic nanoparticles and shells covering them) are determined. Since the pioneering work of Stoner and Wolfforth over six decades ago, the behavior of magnetic single (or mono) domain particles has held enormous fascination. Magnetization reversal in such single domain particles occurs often via coherent rotation of spins. As a consequence of this rotation mechanism, magnetic nanoparticles show high co-ercivities, which lie between those of soft and hard permanent magnetic materials. The ability to control the magnetism in these types of particles makes them very attractive for applications, for example, in information storage. Moreover, the research on magnetic nanoparticles has raised hopes for applications in the fields of biology and medicine; for example, drug targeting, cancer therapy, lymph node imaging, hyperthermia, and so forth.

Keywords: *Single Domain, Magnetic Nanoparticles, Reactions, Magnetic Fields, Mechanical factors, macro molecules*

INTRODUCTION

The use of magnetic nanoparticles (MNPs) and suspensions containing such particles in biomedicine has expanded in recent years, along with their engineering applications [1–5]. The main areas of application in the former case encompass contrast enhancement in magnetic resonance imaging, the early diagnosis of diseases, the targeted delivery and controlled release of drugs, the purification and separation of various biological substances, and therapy against malignant tumors by means of magnetic hyperthermia or a combination of hyperthermia with chemotherapy and radiotherapy [6–17]. An innovative nano-mechanical approach to con trolling the biochemical properties of macromolecules (MMs) (e.g., enzymes (specific protein biocatalysts) attached to MNPs) through exposure to low frequency (f 10 kHz) alternating magnetic fields (AMFs). This concept employs MNPs to convert magnetic field energy into deformation and conformational changes of macro molecules attached to particles, rather than using the particles as heat sources. The first encouraging results obtained using these Nano-mechanical approaches were reported in [20, 21]. It may be regarded as the basis of an innovative technological platform for targeted drug delivery, remote controlled drug release from Nano containers and Nano gels, manipulation of drug activity, and control of the kinetics of biochemical reactions in vitro and in vivo. It is therefore necessary to consider a number of questions regarding the optimization of MNP parameters; the design of MNP based aggregates, and the characteristics of AMFs that ensure the best Nano mechanical action of a field on the structure and bio chemical properties of MMs. The aggregates in question usually contain a magnetic nucleus with radius RM covered by several shells: a shell of gold preventing MNP toxicity (this shell can be replaced with or complemented by a polymer or ceramic shell), a linker shell, and a functional shell (Fig. 1). The gold shell enables the formation of strong covalent bonds with the polymer linkers, which are subsequently used to attach different functional MMs to the particles. The MMs perform a predetermined set of functions encompassing the recognition of specific targets on cell membranes, early diagnosis, visualization, therapy, etc. A hydrodynamic radius RHD below several tens of nanometers is one condition for MNP use in medicine; due to these size limitations, all MNPs available for medical use are single domain MNPs (SMNPs). The aim of this work was to substantiate theoretically these new Nano mechanical approaches to con trolling biochemical reactions using low

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frequency (non-heating) AMFs. The optimum AMF parameters are found, along with those of the magnetic nuclei and various shells of SMNPs and their aggregates enabling effective Nano mechanical control over bioactive macromolecules.

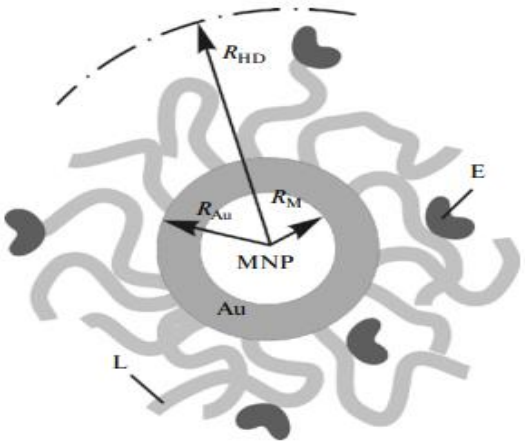

Fig. 1. Typical design of a magnetic nanoparticle (MNP) for Nano medical applications. E is an enzyme macromolecule, L is a linker. RM, RAu, and RHD are the radii of the magnetic core, the gold shell, and the hydrodynamic resistance, respectively

DYNAMICS OF MAGNETIC NANOPARTICLES IN AMF

SMNP dynamics in a suspension exposed to AMFs is generally determined by a multitude of factors that are enumerated and briefly characterized below. The value and rate of change in mechanical torque L exerted on an SMNP by a uniform AMF and those of force F exerted by a nonhomogeneous AMF are of critical importance. The instantaneous value of L is in turn determined by the current magnetic field induction B, magnetization J, and the volume of the SMNP, along with angle θ between vectors and (see below). An external magnetic field tends to order the magnetic moments of the SMNP, while thermal fluctuations tend to randomize them. The group of hydrodynamic forces is next in importance. It includes the viscous friction force exerted by the environment on a SMNP rotating in an AMF and the force exerted by a fluid stream moving relative to the SMNP. The capture of a certain amount of liquid from the environment by the particle (increasing the effective hydrodynamic radius and mass of the particle), along with the Brownian dynamics of particles and their physicochemical interaction with the surrounding liquid (Van der Waals, hydrogen and electrostatic bonds) are also of considerable importance. In addition to magnetic and hydrodynamic forces, SMNPs are affected by buoyancy, inertial, and gravitational forces; however, the latter three can be ignored in a first approximation if particles with diameters of less than several tens of nanometers are considered. If an ensemble of closely apposed SMNPs is considered, dipole–dipole (magneto static) forces and the exchange interaction must be taken into account; however, both are negligible in the case of particles with nonmagnetic coatings several nanometers thick (which is typical of SMNPs used in medicine). The role of the magneto static interaction is minor as well if particles with radii RM appreciably lower than half the distance between them and exposed to an external AMF with B 0.01 T at room temperature are considered. To a first approximation, the dynamics of rotational motion of the SMNP is thus determined by the action of the forces produced by an external AMF, the viscous resistance of the environment, and the resistance of attached MMs to deformation.

If SMNPs with radii RM 6–10 nm are considered, we must allow for the contribution from near surface magnetic anisotropy, which increases as RM diminishes and can be included by introducing an additional term KsS into (1), where Ks is a coefficient of surface anisotropy and S is the lateral surface area of the MNP. Elongated SMNPs have an additional char acteristicbesides crystallographic and surface anisotropy: geometric anisotropy, which is determined by the particle's shape and aspect ratio Φ = l/d (where l is the length of the MNP, and d is its diameter in a plane perpendicular to the major axis). At Φ ——————— 1, the contribution from geometric anisotropy to the magnetic characteristics of the MNP can exceed those of the surface and crystallographic anisotropy.

NANOMECHANICS OF MACROMOLECULES

Viscoelastic deformation characteristics and the parameters of discontinuous conformational transitions resulting from applied force are of extreme importance to the chemical and catalytic properties of macromolecules, and for their biological functions. These characteristics influence the course of multiple processes, including catalysis, inhibition, recognition, attachment, transcription, and replication. The range of forces relevant to monomolecular manipulation and research on pairwise interaction between MMs (e.g., DNA–Protein, enzyme–substrate, RNA–polymerase or topoisomerase) is limited by the thermal motion from below and the covalent bond strength from above. It is easy to see that the average product of force FT generated during thermal vibrations in a harmonic oscillator and absolute deformation Δx inside it is kBT, i.e. 1.38 × 10–23 × 293 ≈ 4.1 × 10–21 J ≈ 4.1 pN nm at room temperature, since the distribution of energy among the degrees of freedom is

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uniform. Consequently, the root mean square of the force's noise component lies in the range 0.4– 4 pN, if deformations Δx in the 1–10 nm range characteristic of macromolecules are considered. The upper limit of the molecular forces is the strength of the covalent bond and therefore ranges from 1000 pN to 2000 pN. The range of force described above can currently be reproduced by the hydrodynamic stretching of MMs, optical and magnetic tweezers, and atomic force microscopes.

MECHANOCHEMISTRY AT THE SINGLE MOLECULE LEVEL

Mechanochemistry and mechanical activation as a branch of chemical technology have been known for hundreds of years. However, methods and equipment for the experimental investigation of the pathways and mechanisms by which mechanical deformations affect the structure and chemical properties of single macromolecules have become available only within the last 15–20 years. This field of research is generally referred to as single molecule force spectroscopy (SMFS). A number of extensive works describe the techniques used in SMFS and the results obtained in this field. The most developed and widely applied SMFS methods can be divided into four groups (Fig. 2): the modified contact mode of atomic force microscopy (AFM), optical (OP) and magnetic/electromagnetic (MP) tweezers, and electrophoresis through Nano pores (NPE).

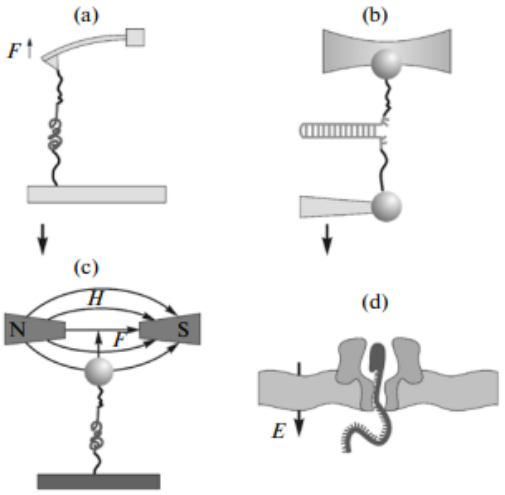

Fig. 2. Four ways of performing single molecule force spectroscopy on macromolecules: (a) atomic force microscopy, (b) laser optical tweezers, (c) magnetic tweezers, (d) Nano porous membrane.

Each of these four groups has its own features and several modifications, and together they cover almost the entire area of interest on the force deformation event map in the dynamics of macromolecules (Fig. 3).

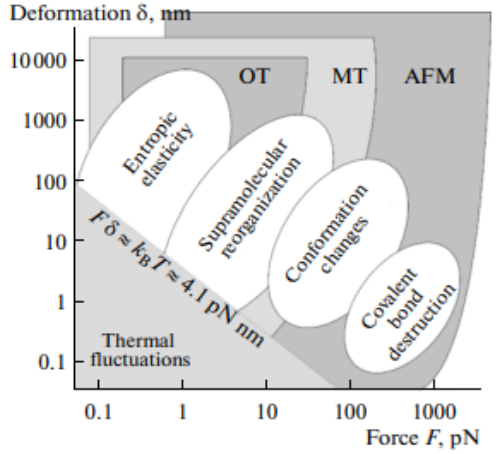

Fig. 3. Force deformation map of intermolecular processes in macromolecules and methods available for studying these processes. AFM is atomic force microscopy; OT and MT are optical and magnetic tweezers, respectively

Studies conducted during the initial stage of SMFS development were mainly devoted to the dynamic and relaxation Nano mechanical characteristics of MMs; however, the number of studies dedicated to studying the atomic and molecular mechanisms of chemical and catalytic reactions at the level of individual MMs has grown considerably in recent years. A number of works have presented miscellaneous data on changes in the conformation of individual MMs as a result of applied force and the resulting changes in the pathways and rates of reactions involving these molecules. If there is no external force, the energy supplied by thermal fluctuations is in most cases sufficient to traverse only the lowest energy barriers. This determines the reaction scenario, while the application of force can alter the reaction trajectory (Fig. 4) due to the selective reduction of certain barriers by $\Delta U \approx F\Delta x$, where Δx is the deformation of interatomic bonds. An example illustrating the effect of tensile force produced by an AFM probe on the activity of the enzyme thioredoxin is shown in Fig. 5a, and the dependence of the kinetics of the enzymatic reaction on AFM induction B (and hence force FM proportional to B) in a magnetic suspension containing magnetite nanoparticles with attached chymotrypsin MMs is qualitatively similar (Fig. 5b). The non-monotonous character of these dependences is probably due to the occurrence of competing processes that depend on the force being applied in a different manner (e.g., the deformation and destruction of weak bonds in MMs).

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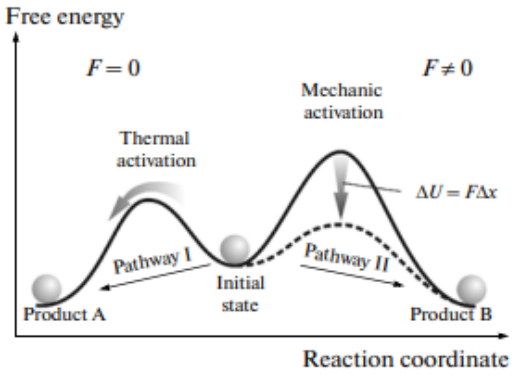

Fig. 4. Two possible pathways for a chemical reaction: (I) with no mechanical deformation (thermal activation only); (II) under the impact of applied force F.

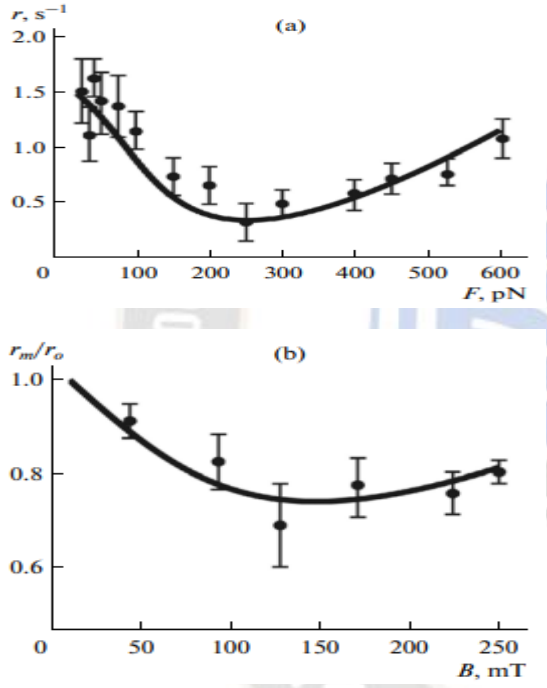

Fig. 5. Dependence of thioredoxin activity (a) on applied force F and the dependence of chymotrypsin activity (b) of magnetic field induction B; in the latter, forces proportional to B are induced in a molecule

POSSIBLE MOLECULAR MECHANISMS OF AMF EFFECT ON THE KINETICS OF MACROMOLECULAR REACTIONS IN MAGNETIC NANOSUSPENSIONS

From the general concepts of and results obtained by SMFS, we may conclude that mechanical forces and deformations can affect the pathways and kinetics of chemical and enzymatic reactions in multiple ways. The ones that currently seem obvious are listed below with brief comments:

1. MMs linked to SMNPs in an aggregate can undergo extension, compression, torsion and shear deformations as the magnetic particles rotate in an alternating MF; the type of deformation depends on MM localization in the aggregate relative to the SMNP. The elastic deformation of a macromolecular chain changes the interatomic distances and angles between bonds; the entropy and mobility of the chain decline, while its free energy rises. This can have a considerable impact on the mechanisms and rates of biochemical reactions involving MMs.

2. Changes in the interatomic distances and active site configurations in an enzyme or inhibitor can dramatically alter the activity of these molecules.

3. Changes in the conformation of an MM and its secondary, tertiary, or quaternary structure that occur as the critical value (typically several tens to several hundreds of piconewtons) of force is achieved can abruptly change its chemical properties.

4. The breaking of covalent bonds joining MMs to SMNPs or linkers, or the destruction of strong bonds within the MM itself as the second critical value of the acting force (~103 pN) is achieved, abruptly discontinues the action of the force on MMs.

5. Let us presume that a certain bimolecular reaction requires a search for specific sites of individual functional groups' localization within a macromolecule relative to certain groups in a second macromolecule. This is followed by positioning, attachment, activation (initiation), and other successive stages, with each stage having its characteristic duration. Stereo selectivity is typical of catalytic (enzymatic) reactions. The movement of a MM attached to a SMNP, relative to another MM attached to a different SMNP or to molecules in solution, can reduce the time spent in reaction cells by interacting groups; on the other hand, it can increase the frequency of molecular encounters, relative displacement, and reorientation. The reaction conditions can thus either deteriorate or improve after an MF is applied (depending on the ratio of the rates and the characteristic times in the system) due to the emerging or lifting of kinetic constraints. In such cases, the MF can obviously play the role of an accelerating or decelerating factor in the reaction. In these and other similar situations, the value of the forces applied to the molecules is not of decisive importance; those forces that must be exceeded for the relative position of the molecules to change are in fact very weak (e.g., hydrogen bond and Van der Waals forces) it is thought that the macromolecular topo-chemical and kinetic mechanisms of MF action are especially relevant for reactions involving

enzymes and inhibitors, supramolecular complexes, DNA, RNA, and so on.

6. Let us consider one final factor that can change the macro kinetics of a reaction occurring in an AMF with magnetic nanoparticles suspended in solution: The presence of magnetic nanoparticles in the liquid and the periodic changes in particle orientation caused by the AMF (with the frequency of field alter nation) or continuous rotation in a rotating magnetic field can also change the conditions of diffusion in the reaction zone of nanoscale size. The rate constants for diffusion limited reactions can therefore change when an MF is applied.

CONCLUSION

We have presented a widely applicable way of con trolling biochemical reactions in suspensions containing SMNPs and any macromolecules attached to them. It is based on Nano mechanical processes induced by a low frequency (non-heating) magnetic field in the reaction cells close to magnetic nanoparticles; these processes can be described as deformation and conformational changes in macromolecules attached to the nanoparticles, changes in the relative positions of macromolecules (or individual active groups), and the acceleration of molecule diffusion. The effects of certain mechanisms depend primarily on the dynamic deformation properties of MMs, and on the dynamic characteristics of SMNPs and aggregates they are incorporated. Magneto mechanical spectroscopy of relaxation processes in a system can yield information on the elementary acts and intermediate states inside; it can also be used to study the atomic and molecular mechanisms of catalysis and active site functioning in enzyme macromolecules. From a practical point of view, the use of Nano mechanical approaches in medicine allows the development of innovative techniques for the targeted delivery of new generation drugs and the remote control of drug release and activity.

REFERENCES

[1] Magnetic Nanoparticles. From Fabrication to Clinical Application, Thanh, N.T.K., Ed., Boca Raton: CRC Press, 2012.
[2] Microfluidic Technologies for Human Health, Demeric, U., et al., World Sci., 2013.
[3] Magnetic Nanomaterials, Kumar, C.S.S., Ed., Wein heim: VCH Verlag, 2009.
[4] Reddy, L., Areas, J.L., Nicolas, J., and Couvreur, P., Chem. Rev., 2012, vol. 112, p. 5818.
[5] Kim, J.E., Shin, J.Y., and Cho, M.H., Arch Toxicol., 2012, vol. 86, p. 685.
[6] Shi, D., Bedford, N.M., and Cho, H.S., Small, 2011, vol. 7, p. 2549.
[7] Jeyadevan, B., J. Ceram. Soc. Jpn., 2010, vol. 118, no. 6, pp. 391–401.
[8] Milani, V., Lorenz, M., Weinkauf, M., et al., Int. J. Hypertherm., 2009, vol. 25, no. 4, pp. 262–272.
[9] Hoare, T., Timko, B.P., Santamaria, J., et al., Nano Lett., 2011, vol. 11, no. 3, pp. 1395–1400.
[10] Thomas, C.R., Ferris, D.P., Lee, J.H., et al., J. Am. Chem. Soc., 2010, vol. 132, pp. 10623–10625.
[11] Peiris, P.M., Bauer, L., Toy, R., et al., ACS Nano, 2012, vol. 6, no. 5, pp. 4157–4168. 12. Thomas, C.R., Ferris, D.P., Lee, J.H., et al., J. Am. Chem. Soc., 2010, vol. 132, pp. 10623–10625.
[12] Yoo, D., Jeong, H., Preihs, C., et al., Angew. Chem. Int., 2012, vol. 51, pp. 12482–12485.
[13] Laurent, S., Dutz, S., Hafeli, U.O., and Mahmoudi, M., Adv. Colloid Interface Sci., 2011, vol. 166, pp. 8–23.
[14] Cherukuri, P., Glazer, E.S., and Curley, S.A., Adv. Drug Deliv. Rev, 2010, vol. 62, pp. 339–345.