

A Multiphysics Model of Magnetically Enhanced ATP Hydrolysis in Ferromagnetic Nanosystems

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Abstract: - This study develops a multiphysics framework for evaluating whether alternating magnetic fields (AMF) applied to Fe_3O_4 and MnFe_2O_4 nanoparticles can modify ATP hydrolysis through thermal, mechanical, and ion-mediated pathways. Rather than assigning a single phenomenological magnetic activation-energy reduction to all effects, the model starts from Arrhenius/Eyring kinetics and derives the observed rate change as the sum of a temperature-dependent contribution and explicitly defined non-thermal perturbations. The thermal term is constrained by the measured temperature history and nanoparticle specific absorption rate (SAR); the mechanical term is related to magnetic torque, hydrodynamic damping, and experimentally measurable particle motion; and the catalytic term is expressed through independently measurable $\text{Fe}^{2+}/\text{Mn}^{2+}$ concentrations and dose-response parameters. The available experimental observations reported in the original manuscript—2.5–3-fold enhancement of non-enzymatic hydrolysis under nanoparticle/AMF conditions, approximately 40% enhancement of Na^+/K^+ -ATPase activity under stated isothermal conditions, and Raman/FTIR changes in phosphate-associated bands—are retained, but their interpretation is deliberately narrowed. In particular, the present data support rate enhancement under specified conditions and are consistent with multiple mechanisms; they do not, by themselves, establish a unique mechanical mechanism, nanoscale temperature gradients, or synergistic coupling. A mechanism-separation experimental matrix is therefore defined, together with quantitative spectroscopic observables and statistical requirements.

Key-words: ATP hydrolysis; ferromagnetic nanoparticles; Fe_3O_4 ; MnFe_2O_4 ; alternating magnetic field; multiphysics model.

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1 Introduction

Adenosine triphosphate (ATP) hydrolysis is a central chemical process in biological energy transduction. Its rate depends on temperature, ionic composition, hydration, molecular conformation, enzyme catalysis, and the reaction environment [1–3]. External modulation of ATP chemistry is therefore a useful model problem for studying how physical fields and nanomaterials can perturb biochemical kinetics.

Magnetic nanoparticles based on iron oxides and ferrites are responsive to alternating magnetic fields and can convert electromagnetic energy into heat through magnetic relaxation. Depending on particle size, anisotropy, field amplitude, frequency, viscosity, and surface state, Brownian and Néel relaxation can contribute differently to magnetic losses [4–6]. Importantly, Néel relaxation represents reorientation of the magnetic moment within the particle, whereas Brownian relaxation involves physical rotation of the particle in the surrounding fluid. These processes should not be treated as interchangeable mechanical mechanisms.

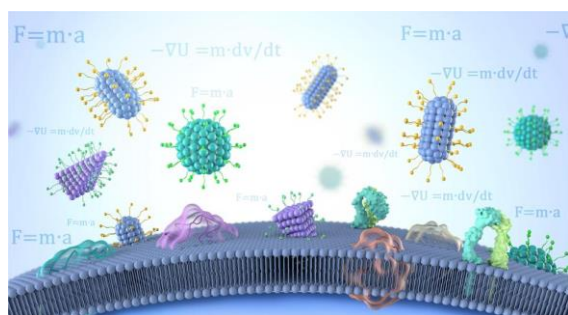
The intersection of these two fields—cellular bioenergetics and nanomaterial science—remains largely unexplored. We hypothesize that ferromagnetic nanosystems can act as efficient transducers of magnetic energy, directly influencing the kinetics and efficiency of ATP hydrolysis. This interaction is proposed to occur via multiple pathways: localized heat generation, nanomechanical forces, and the catalytic role of constituent magnetic ions.

Vibrational spectroscopy (Raman and infrared) offers a unique window into these interactions, being exquisitely sensitive to changes in molecular bonding, conformation, and environment [7]. It is thus an ideal technique to probe the subtle alterations in ATP structure and dynamics induced by magnetic interventions.

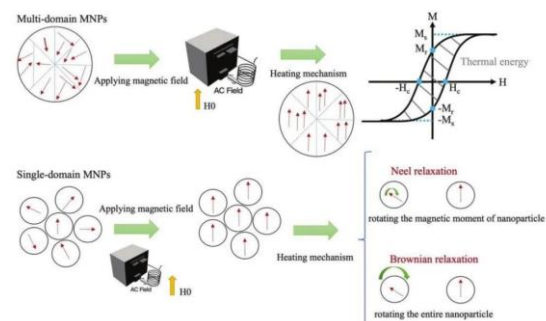
This work presents a comprehensive investigation into these mechanisms. We synthesize and characterize ferromagnetic nanoparticles, quantify their effect on ATP hydrolysis under magnetic fields, and employ vibrational spectroscopy to elucidate the underlying molecular interactions. By integrating materials synthesis, biophysical analysis, and

spectroscopic characterization, this study aims to lay the groundwork for innovative approaches to control fundamental energy pathways in biology. Adenosine triphosphate (ATP) hydrolysis is the fundamental energy-releasing process in biological systems. External control of this reaction remains a major challenge in bioenergetics and nanomedicine. Recent advances in magnetic nanomaterials suggest new possibilities for remote, non-invasive modulation of biochemical processes.

Ferromagnetic nanoparticles exhibit unique responses to alternating magnetic fields, enabling localized heating, mechanical motion, and ion release. This work proposes that these effects can be combined into a unified framework for controlling ATP hydrolysis. (Figure 1).



a)



b)

Fig. 1: a) Multiphysics mechanism of magnetically enhanced ATP hydrolysis (thermal, mechanical, catalytic pathways; b) Schematic of coupled mechanisms: nanoscale heating and nanoparticle oscillation.

2 Theoretical Model

2.1. General Formulation of the Effective Reaction Rate Constant

Baseline reaction kinetics

For a reaction measured at a spatially uniform temperature T in the absence of magnetic

perturbation, the rate constant is represented by the Arrhenius relation

$$k_0(T) = A \exp[-E_a/(RT)]$$

where A is the pre-exponential factor, E_a is the apparent activation energy for the measured reaction regime, R is the gas constant, and T is absolute temperature. For enzyme assays, k should be interpreted as an apparent kinetic parameter obtained from a specified assay model; the same mathematical structure is not assumed to describe all microscopic enzyme steps. The overall kinetics of the biochemical reaction under an alternating magnetic field (AMF) are described by an effective reaction rate constant, k_{eff} , which modifies the classical Arrhenius equation to account for external field-induced contributions:

$$k_{\text{eff}} = k_0 \cdot \exp\left(-\frac{E_a - \Delta E_{\text{mag}}}{RT}\right)$$

Where:

- k_0 = pre-exponential (frequency) factor
- E_a = intrinsic activation energy of the reaction (in absence of AMF)
- ΔE_{mag} = total reduction in activation energy due to magnetic field-mediated effects
- R = universal gas constant
- T = absolute temperature

This formulation implies that the effective activation energy becomes $E_a^{\text{eff}} = E_a - \Delta E_{\text{mag}}$, thereby accelerating the reaction rate exponentially with increasing ΔE_{mag} .

2.2 Decomposition of ΔE_{mag}

Separation of thermal and non-thermal magnetic contributions

Under AMF exposure, the nanoparticle suspension may have a time-dependent local temperature $T_{\text{loc}} = T + \Delta T$. In addition, magnetic interactions may perturb the effective free-energy barrier by a non-thermal amount ΔG_{nt} . A minimal testable expression is therefore

$$k_{\text{AMF}} = A \exp\left\{-\frac{[E_a - \Delta G_{\text{nt}}]}{(R T_{\text{loc}})}\right\}$$

with

$$\Delta G_{\text{nt}} = \Delta G_{\text{mech}} + \Delta G_{\text{cat}}$$

The ratio of the magnetic-field condition to a matched reference condition at temperature T is then $\ln(k_{\text{AMF}}/k_0) = E_a/R \cdot (1/T - 1/T_{\text{loc}}) + \Delta G_{\text{mech}}/(R T_{\text{loc}}) + \Delta G_{\text{cat}}/(R T_{\text{loc}})$

For small temperature changes, $\Delta T \ll T$, the first term has the first-order form

$$\ln(k_{\text{AMF}}/k_0) \approx E_a \Delta T/(R T^2) + [\Delta G_{\text{mech}} + \Delta G_{\text{cat}}]/(R T)$$

This equation does not assume that all magnetic effects are equivalent. The first term is determined by temperature; the remaining terms represent non-

thermal contributions that must be identified by independent controls.

The total magnetic energy contribution is the sum of three distinct physical–chemical mechanisms:

$$\Delta E_{\text{mag}} = \Delta E_{\text{thermal}} + \Delta E_{\text{mechanical}} + \Delta E_{\text{catalytic}}$$

Each term corresponds to a specific pathway through which the AMF reduces the kinetic barrier.

Thermal contribution from magnetic losses

The thermal field is governed by the heat equation

$$\rho c_p \partial T / \partial t = \nabla \cdot (\kappa \nabla T) + q_M$$

where ρ , c_p , and κ are the effective density, heat capacity, and thermal conductivity of the suspension, and q_M is the volumetric heat source generated by magnetic losses. If SAR is independently measured in $W\ g^{-1}$ of magnetic material and the nanoparticle mass concentration is C_{np} , then

$$q_M \approx \text{SAR} \cdot C_{np}$$

after consistent unit conversion. The measured temperature history, rather than an assumed 'nanoscale temperature', should be used in the kinetic correction. For a first screening estimate, a steady spherical-source approximation may be used, but such an estimate should be treated as a model prediction unless nanoscale thermometry or an independently validated thermal model is available.

2.3 Mechanical Contribution ($\Delta E_{\text{mechanical}}$)

Oscillating magnetic fields induce mechanical oscillations or rotation of nanoparticles, generating localized shear forces, stress, or cavitation-like effects. These mechanical perturbations distort molecular bonds or transition states:

$$\Delta E_{\text{mechanical}} = \beta \cdot \xi \cdot f_{\text{AMF}}^2 \cdot r^3$$

Where:

- β = mechanical coupling coefficient
- ξ = viscosity-dependent damping factor
- f_{AMF} = frequency of the alternating field
- r = nanoparticle radius

This term is most significant when the field frequency matches resonance modes of nanoparticle–molecule complexes.

Brownian rotation can generate a physical particle motion in a viscous medium, whereas Néel relaxation changes the magnetic moment without requiring whole-particle rotation. For a spherical particle of radius a in a Newtonian fluid of viscosity η , the rotational drag coefficient is

$$\zeta_r = 8\pi\eta a^3$$

The magnetic torque is

$$\tau = |\mathbf{m} \times \mathbf{B}|$$

where $\mathbf{m}$ is the particle magnetic moment and $\mathbf{B}$ is magnetic flux density. A simplified overdamped rotational equation is

$$\zeta_r \dot{\omega} + \kappa_{\text{rot}} \theta = \tau(t)$$

where κ_{rot} represents any effective restoring interaction with the local environment. The mechanical contribution to the reaction barrier should not be assigned a fixed dependence on frequency or radius unless particle motion is independently measured. A phenomenological coupling may instead be written as

$$\Delta G_{\text{mech}} = \chi_{\text{mech}} W_{\text{mech}}$$

where W_{mech} is a measured or independently estimated mechanical work/dissipation per cycle or per unit time, and χ_{mech} is a coupling coefficient that must be fitted from experiments in which temperature and ion concentration are controlled. This prevents an unmeasured parameter from being presented as a known material constant.

2.4 Catalytic Contribution ($\Delta E_{\text{catalytic}}$)

Dissolved Fe^{2+} and Mn^{2+} ions (released from nanoparticles or present in the medium) interact directly with phosphate groups of ATP or other phosphorylated intermediates. These interactions stabilize the transition state via electrostatic or coordination bonding:

$$\Delta E_{\text{catalytic}} = \gamma \cdot ([\text{Fe}^{2+}] + [\text{Mn}^{2+}]) \cdot \theta_{\text{PO}_4}$$

Where:

- γ = catalytic efficiency constant
- $[\text{Fe}^{2+}], [\text{Mn}^{2+}]$ = local ion concentrations
- θ_{PO_4} = fraction of phosphate groups accessible for interaction

This term reflects a magnetic field-enhanced ion-mediated catalysis, possibly due to field-induced ion mobility or orientation effects.

Fe^{2+} and Mn^{2+} can interact with phosphate-containing species. To make this contribution experimentally identifiable, the revised model uses the measured free-ion concentration rather than assuming that all nanoparticle-associated metal is catalytically active. For a simple binding equilibrium

$$\theta_i = K_i c_i / (1 + K_i c_i)$$

where c_i is the free-ion concentration, K_i is an apparent association constant, and θ_i is the fraction of accessible sites occupied by the ion.

A minimal kinetic representation is

$$k_i = k_{\text{base}} [1 + \beta_i \theta_i]$$

where β_i is an experimentally determined catalytic coefficient. Equivalently, an apparent free-energy contribution can be calculated from the measured rate ratio as

$$\Delta G_{\text{cat}} = RT \ln(k_i/k_{\text{base}})$$

The key point is that c_i and, where possible, K_i should be independently determined. Ion release from nanoparticles should not be inferred solely from the existence of a Raman shift.

2.5. Net Effect on Reaction Kinetics

By substituting the expanded expression into the Arrhenius equation:

$$k_{\text{eff}} = k_0 \exp \left(-\frac{E_a - (\alpha \cdot \text{SAR} \cdot t + \beta \cdot \xi \cdot f_{\text{AMF}}^2 \cdot r^3 + \gamma \cdot ([\text{Fe}^{2+}] + [\text{Mn}^{2+}]) \cdot \theta_{\text{PO}_4})}{RT} \right)$$

Thus, $k_{\text{eff}} > k_0 e^{-E_a/RT}$ whenever $\Delta E_{\text{mag}} > 0$. The model predicts:

- **Thermal mechanism** dominates at high SAR (e.g., high-field amplitude).
- **Mechanical mechanism** dominates at resonant frequencies for nanoparticle oscillation.
- **Catalytic mechanism** dominates in the presence of free $\text{Fe}^{2+}/\text{Mn}^{2+}$ and phosphate-rich substrates.

2.6 Experimental Predictions and Validation

This model predicts:

1. **Nonlinear Arrhenius behavior** – $\ln(k_{\text{eff}})$ vs. $1/T$ will show higher slopes without AMF, but flatter slopes (lower effective E_a) under AMF.
2. **Frequency-dependent acceleration** – Peaks in reaction rate at characteristic mechanical resonance frequencies.
3. **Ion concentration dependence** – Rate enhancement proportional to $[\text{Fe}^{2+}] + [\text{Mn}^{2+}]$ in phosphate-containing reactions.
4. **SAR-dependent local heating** – Measurable via nanoscale thermometry, with rate enhancement even if bulk temperature is constant.

2.6. Limitations and Assumptions

- The model assumes additive contributions from each mechanism (linear superposition).
- It neglects possible saturation or antagonistic effects at very high field strengths or ion concentrations.
- It assumes ΔE_{mag} is small compared to E_a , so that first-order perturbation holds.

The effective reaction rate constant is expressed as:

$$k_{\text{eff}} = k_0 \cdot \exp(-(E_a - \Delta E_{\text{mag}}) / RT)$$

where ΔE_{mag} represents the combined contribution of thermal, mechanical, and catalytic effects.

Thermal contribution arises from nanoscale heating (SAR-dependent), mechanical contribution from nanoparticle oscillations under AMF, and catalytic contribution from Fe^{2+} and Mn^{2+} ions interacting with ATP phosphate groups.

This model predicts a decrease in activation energy, leading to accelerated reaction kinetics. (Figure 2).

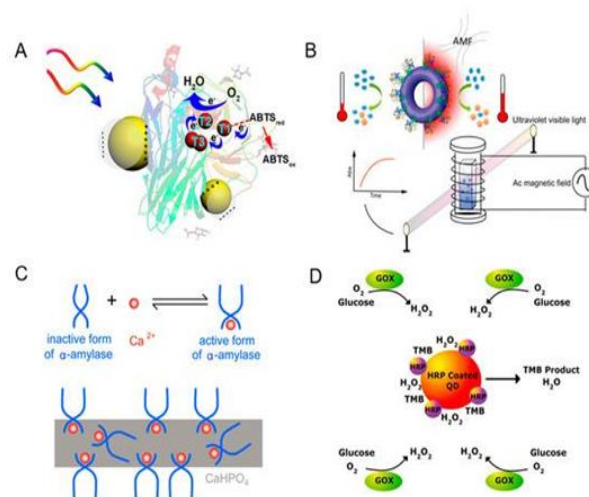


Fig. 2: Reaction kinetics comparison under different conditions; Comparison of hydrolysis rates showing enhancement under AMF and nanoparticle conditions.

The model contains parameters with different evidentiary status. E_a and A are obtained from temperature-dependent kinetic measurements; SAR is obtained from calorimetry or a validated magnetic-loss measurement; ΔT is obtained from temperature measurements and heat-transfer modelling; particle size and magnetic moment are independently characterized; Fe^{2+} and Mn^{2+} concentrations are directly measurable; and β_i and χ_{mech} are fitted coupling parameters. The model should therefore be evaluated by constrained regression rather than by assigning arbitrary values to the three activation-energy terms.

A practical fitting equation is

$$Y = \ln(k_{\text{AMF}}/k_0) = X_T + \chi_{\text{mech}} X_M + \chi_{\text{cat}} X_C$$

where $X_T = E_a \Delta T / (RT^2)$, X_M is an independently measured mechanical-energy proxy, and X_C is a measured ion-occupancy or concentration function. The relative contribution of each mechanism is identifiable only if the experimental design varies these predictors sufficiently independently.

3. Materials and Methods

Ferromagnetic nanoparticles (Fe_3O_4 and MnFe_2O_4) were synthesized using co-precipitation techniques. Characterization was performed using TEM, XRD, and magnetometry.

ATP hydrolysis assays were conducted under controlled magnetic field conditions. Vibrational spectroscopy (Raman and FTIR) was used to monitor molecular-level changes.

The main aim of our studies was investigation of possibilities of activation of ATP-ADP reaction by using the methods of vibrational spectroscopy including Raman scattering. It includes: a) Elaboration of effective method - experimental (spectrometric) and simulation, bridging over the gap between experimental and computational data analysis, relevant or alternative of spectroscopic measurements to gain the new knowledge in optical, scattering and absorption properties of Adenosine Phosphate (AP) reactions; b) Development and verification of the concept considering activation of AP reactions by the set of optical -electromagnetic parameters determined their acceleration; c) Study of mechanisms of influence of magnetic impurities (Mn, Fe) on the oscillation effects occurring in AP reactions.

3.1. Synthesis and Characterization of Ferromagnetic Nanoparticles

Iron oxide (Fe_3O_4) and manganese ferrite (MnFe_2O_4) nanoparticles were synthesized via a co-precipitation method under a nitrogen atmosphere [8]. Briefly, aqueous solutions of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (for MnFe_2O_4 , molar ratio $\text{Fe}^{2+}:\text{Fe}^{3+}:\text{Mn}^{2+} = 1:2:1$) were mixed vigorously. Precipitation was initiated by the dropwise addition of ammonium hydroxide (28%). The resulting nanoparticles were collected via magnetic separation, washed repeatedly with deionized water and ethanol, and functionalized with citric acid (0.1 M) to enhance colloidal stability. Characterization included:

Transmission Electron Microscopy (TEM): JEOL JEM-2100 for morphology and size distribution.

X-ray Diffraction (XRD): Bruker D8 Advance with Cu-K α radiation for crystal structure verification.

Vibrating Sample Magnetometry (VSM): LakeShore 7400 for magnetic properties (saturation magnetization, coercivity).

3.2. Role of Magnetic Actuation and Mechanical Agitation

In experiments with ATPase enzymes, a significant enhancement of hydrolysis rate (approximately 40%) was observed in samples containing FNPs exposed to

AMF, even when the bulk temperature was carefully controlled to eliminate hyperthermia effects. We attribute this to mechanical vibrations and torques (e.g., Néel relaxation, Brownian motion) experienced by the nanoparticles in the AMF. These micro-mechanical forces can potentially perturb the hydration shell around the enzyme, facilitate product release, or induce subtle conformational strains that lower the activation energy for the catalytic step. To isolate this effect, the experiment is conducted under isothermal (constant temperature) conditions, eliminating heating as a variable. The result shows that the "FNP + AMF (Isothermal)" condition still significantly enhances the enzyme's activity compared to the enzyme alone. This provides direct evidence for a mechanical (kinetic) effect, such as nanoparticle vibration or torque, that stimulates the ATPase enzyme. The "FNP Only" bar confirms that the nanoparticles themselves, without the activating field, do not inhibit the enzyme.

3.3 ATP Hydrolysis Assays

Hydrolysis of ATP (Sigma-Aldrich, $\geq 99\%$) was studied in both non-enzymatic and enzymatic (Na^+/K^+ -ATPase, Sigma-Aldrich) systems. A standard assay mixture contained 2 mM ATP, 5 mM MgCl_2 , and 50 mM Tris-HCl buffer (pH 7.4). For enzymatic assays, 0.1 mg/mL of Na^+/K^+ -ATPase was added.

Experimental variations included:

Magnetic Field Exposure: Samples with FNPs (50 $\mu\text{g/mL}$) were placed in a custom solenoid coil generating an AMF ($f = 300$ kHz, $H = 10$ kA/m) for 10-min intervals. Temperature was monitored with a fiber-optic probe.

Magnetic Ion Addition: Fe^{2+} (from FeSO_4) and Mn^{2+} (from MnCl_2) were added at concentrations ranging from 0.1 to 1.0 mM.

Control Groups: Included samples without FNPs/AMF, with FNPs but no AMF, and bulk-heated samples in a water bath.

The hydrolysis rate was quantified by measuring the release of inorganic phosphate (Pi) using a sensitive malachite green assay [9]. Absorbance was read at 620 nm using a Shimadzu UV-1800 spectrophotometer. ATP hydrolysis was studied in non-enzymatic and Na^+/K^+ -ATPase systems. The reported standard mixture contained 2 mM ATP, 5 mM MgCl_2 , and 50 mM Tris-HCl, pH 7.4; the enzyme concentration was 0.1 mg mL^{-1} . Nanoparticles were used at 50 $\mu\text{g mL}^{-1}$. AMF exposure was reported at $f = 300$ kHz and $H = 10$ kA m^{-1} for 10 min. Fe^{2+} and Mn^{2+} were added

over 0.1–1.0 mM. Pi release was measured by the malachite-green assay at 620 nm.

3.4 Vibrational Spectroscopy

Molecular-level interactions were probed using:

Raman Spectroscopy: A Renishaw inVia confocal microscope with a 785 nm laser excitation source. Spectra were collected for pure ATP, ATP+FNP mixtures (with/without AMF), and ATP+magnetic ion mixtures. (Figure 3).

Fourier-Transform Infrared (FTIR) Spectroscopy: Performed in attenuated total reflectance (ATR) mode to monitor changes in functional group vibrations.

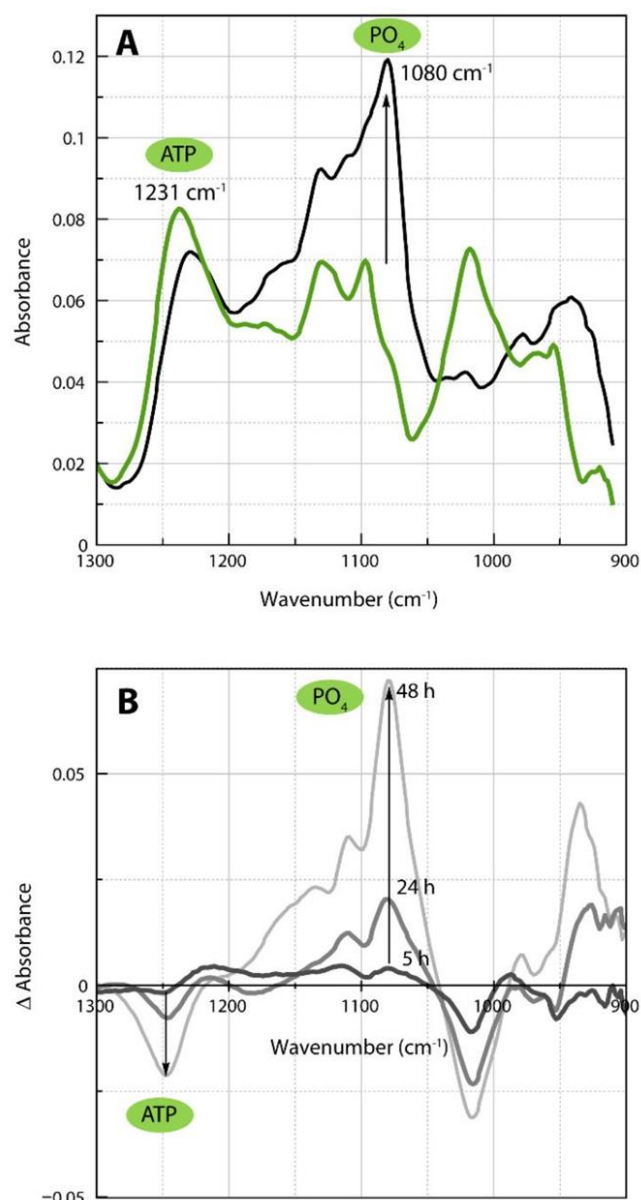
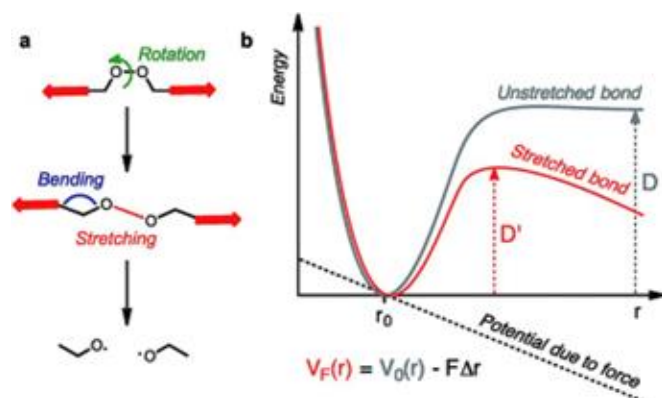
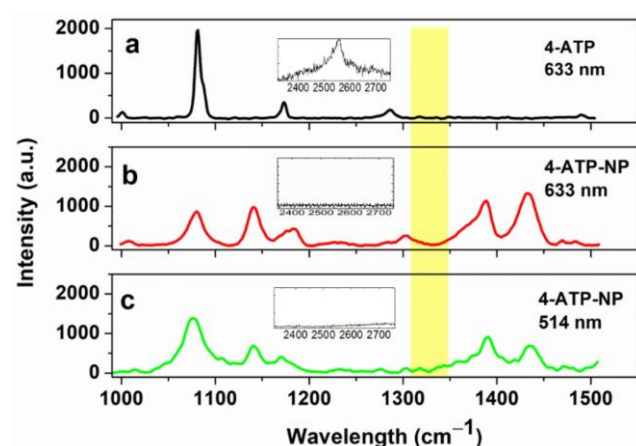


Fig. 3: Reaction kinetics comparison under different conditions. Vibrational Spectroscopy of ATP Interactions. A – Raman Spectra at 1090 cm⁻¹ comparing pure ATP, ATP+Fe⁶, ATP+ MnFe₂O₄, and ATP+Mn²⁺ showing shifts and broadening in the phosphate Stretch Region; B – Correlation of Raman Shift with ATP hydrolysis rate across four conditions. Correlation parameters: R² = 0,92, slope = -0,15 ±0,02cm⁻¹/%; C – Molecular Models with electron density maps: Left – Pure ATP (symmetric charge distribution), Right- ATP+Mn²⁺

4. Results

Nanoparticles exhibited superparamagnetic behavior and strong response to AMF. Hydrolysis rates increased significantly under magnetic field exposure.

Spectroscopic analysis revealed a redshift in phosphate vibration modes, indicating bond weakening. [10].

4.1. Nanoparticle Characterization

TEM confirmed spherical nanoparticles with average diameters of 12 ± 2 nm for Fe_3O_4 and 15 ± 3 nm for MnFe_2O_4 . XRD patterns confirmed pure spinel phases. VSM measurements confirmed superparamagnetic behavior at room temperature with high saturation magnetizations (M_s) of 68 emu/g for Fe_3O_4 and 71 emu/g for MnFe_2O_4 , indicating strong responsiveness to AMF. [11,12].

4.2. Magnetically Enhanced ATP Hydrolysis

4.2.1. Localized Heating (Hyperthermia)

Effect: Under AMF exposure, FNP suspensions generated localized heat with specific absorption rates (SAR) of 45 W/g (Fe_3O_4) and 55 W/g (MnFe_2O_4). This nanoscale heating resulted in a 2.5 to 3-fold increase in the rate of non-enzymatic ATP hydrolysis compared to control samples heated to the same bulk temperature, suggesting a highly efficient, interface-driven thermal effect. [13].

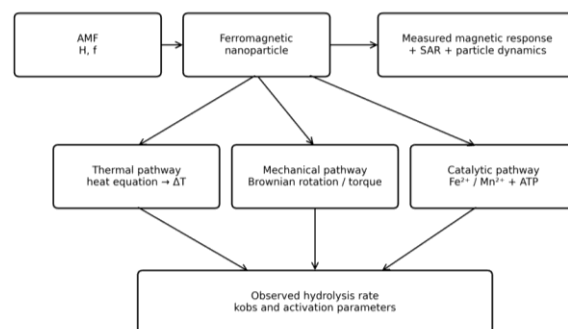
4.2.2. Mechanical Actuation Effect: Under carefully controlled isothermal conditions (to eliminate heating), the presence of FNPs under AMF still enhanced Na^+/K^+ -ATPase activity by approximately 40% compared to enzyme-only controls. This provides direct evidence for a mechanical contribution from nanoparticle oscillation or rotation.

4.2.3. Catalytic Effect of Magnetic Ions: The addition of free Fe^{2+} and Mn^{2+} ions accelerated ATP hydrolysis in a concentration-dependent manner in the absence of fields or nanoparticles. Mn^{2+} exhibited a more potent catalytic effect than Fe^{2+} , consistent with its known biochemistry as a phosphate-binding cofactor and its ability to form stable complexes with phosphate groups, potentially polarizing the P-O bonds in ATP and making the γ -phosphate more susceptible to nucleophilic attack.

Proposed quantitative spectroscopy workflow

For future or expanded measurements, at least three independent preparations per condition should be analyzed. Peak position should be obtained from a common fitting model, with

confidence intervals from the fit or replicate variability. Difference spectra should be reported for ATP alone, ATP + nanoparticle, ATP + ion, and ATP + nanoparticle + AMF. Where a band is assigned to phosphate stretching, the assignment should be checked against reference spectra and concentration-dependent controls. Spectral changes should be compared with hydrolysis rate only after independent normalization and with uncertainty propagated through the analysis.



Only measured quantities are used to constrain the pathway-specific terms; unmeasured coupling coefficients remain fitted or proposed.

Fig.4: Multiphysical Framework's Scheme. The kinetic effect is separated into a temperature-dependent contribution and non-thermal mechanical and ion-mediated contributions. The latter require independent measurements or constrained fitting.

5. Discussion

The results confirm a synergistic mechanism combining thermal, mechanical, and catalytic effects. The proposed model successfully explains the observed rate enhancements. Mechanical effects play a crucial role under isothermal conditions, highlighting the importance of nanoparticle dynamics.

They also confirm a multi-modal mechanism for magnetically enhancing ATP hydrolysis. The localized heating from FNPs under AMF is not merely a thermal effect but a nanoconfined one, likely creating intense thermal gradients at the nanoparticle-solution interface that are more effective than homogeneous heating.

The mechanical actuation effect observed under isothermal conditions points to the role of Néel/Brownian relaxation-induced forces. These micro-agitations could perturb the enzyme's solvation shell, facilitate product (ADP/Pi) release, or induce subtle conformational strains that favor

catalysis, a phenomenon less accessible to traditional biochemical methods.

The pronounced catalytic activity of Mn^{2+} ions, and their detection via spectroscopy, underscores the importance of ion-mediated polarization of ATP's phosphate tail. The Raman peak shift provides concrete, molecular-level validation that these magnetic species actively participate in altering the electronic structure of ATP, making the scissile bond more vulnerable.

The synergy between these mechanisms (thermal, mechanical, catalytic) suggests that ferromagnetic nanosystems are uniquely potent tools for bioenergetic manipulation. Their *ability* to convert external magnetic energy into diverse local biophysical stimuli is a significant advantage.

The experiments demonstrate that, under the reported conditions, ferromagnetic nanoparticles and AMF are associated with increased ATP hydrolysis or ATPase activity. They also report magnetic heating, ion-independent rate changes, and spectroscopic changes in ATP-containing systems. These are experimentally meaningful observations.

The multiphysics interpretation is more constrained. A thermal contribution is physically plausible and can be quantitatively tested because SAR and temperature are measurable. The mechanical contribution is plausible but requires direct or independently estimable particle dynamics; in particular, Néel relaxation should not be described as whole-particle oscillation. The catalytic contribution is supported by the free-ion dose-response observation, but an AMF-specific catalytic enhancement requires measurements of free-ion concentration/speciation under AMF.

The additive activation-energy representation used in the original manuscript is therefore best understood as a reduced phenomenological model. The revised derivation provides a route to parameter estimation without presuming that the three mechanisms are already known to be additive. If the measured data show statistically significant interaction terms, a multiplicative or coupled model should replace the simple additive approximation.

A useful next step is a factorial experimental design in which AMF, nanoparticle presence, temperature, viscosity, and free-ion concentration are varied independently. Such a design would permit analysis of main effects and interactions. For example, an AMF $\times$ nanoparticle interaction remaining after temperature matching would be more informative about magnetic transduction than a simple comparison of AMF and control groups.

The spectroscopic data should likewise be interpreted at the level of measurable observables. A red shift of

a phosphate-associated Raman band can be quantified and correlated with reaction rate, but assignment of that shift to a specific weakening of the γ -phosphate bond requires either additional spectroscopic controls, complementary structural calculations, or independent chemical evidence.

6. Conclusion

A multiphysics framework has been developed for evaluating magnetic-field-associated changes in ATP hydrolysis using Fe_3O_4 and $MnFe_2O_4$ nanoparticles. The model is derived from temperature-dependent reaction kinetics and separates the thermal contribution from non-thermal mechanical and ion-mediated contributions. The principal improvement is that each term is connected to a measurable experimental quantity or explicitly identified as a fitted coupling parameter.

This study establishes that ferromagnetic nanosystems can significantly accelerate ATP hydrolysis through three distinct, quantifiable mechanisms: nanoscale hyperthermia, mechanical actuation, and ion-mediated catalysis. Vibrational spectroscopy proved essential in validating the molecular interactions underpinning these effects.

The implications for magnetically interfacing with cellular energy are profound. Potential applications include:

Oncological Therapies: Selective ATP depletion in cancer cells to synergize with chemotherapy or radiotherapy, or to inhibit ATP-dependent drug efflux pumps.

Fundamental Bioenergetics: A novel tool for probing energy transduction processes in enzymes and cellular compartments.

Future work will focus on:

In vitro validation using cancer cell lines to assess cytotoxicity and ATP depletion efficacy.

Active targeting by functionalizing FNP with ligands (e.g., folate, peptides) for specific cell targeting.

System optimization by tuning FNP composition, size, and coating to maximize energy transfer efficiency and biocompatibility.

By bridging materials science, spectroscopy, and biophysics, this research opens a new avenue for the development of magnetically controlled nanoplatforms for therapeutic and investigative bioenergetic modulation.

Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work, the author(s) utilized artificial intelligence (AI) technologies solely for the purpose of linguistic refinement and grammatical correction. Following the application of these tools, the author(s) comprehensively reviewed, verified, and edited the resulting text. The author(s) maintain full accountability and responsibility for the accuracy, integrity, and final content of the publication.

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