QM/MM Modeling for Enzymatic Reactions

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The Quantum Mechanics/Molecular Mechanics (QM/MM) hybrid approach enables accurate and efficient simulations of enzyme-catalyzed reactions and complex biomolecular systems. By combining quantum mechanics to describe reactive regions with molecular mechanics for the surrounding environment, QM/MM provides a powerful framework for studying chemical transformations in large systems. Core concepts related to QM/MM modeling include QM/MM partitioning, interaction potentials, boundary treatments, and embedding schemes such as mechanical, electrostatic, and covalent embedding. The investigation of enzymatic mechanisms, such as the chorismate mutase reaction and the role of catalytic residues like Arg63, can be utilized by using the QM/MM approach. In the QM/MM approach, advanced techniques such as the Replica Path, Off-Path Simulation, Umbrella Sampling, String, and Nudged Elastic Band (NEB) method are employed to explore reaction pathways and compute free energy barriers.

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ON INVARIANT RINGS OF TYPE II CODES AND NEIGHBORS OF SELF-DUAL CODES

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We study about the weight enumerators of Type II codes and its neighbors, particularly for codes of length 24. Programming implementation is introduced to obtain the coefficient of certain monomials of weight enumerators of codes in genus 2 and 3. We then present the invariant ring constructed by the code d_{24}^+ and its neighbors in genus 1, 2, and 3.

1 Introduction

Definition 1.1. Let $\mathbf{F}_2 = \{0, 1\}$ be the finite field with two elements. The vector space $\mathbf{F}_2^n$ is defined by the inner product

$$u \cdot v = u_1 v_1 + \cdots + u_n v_n$$

for $u = (u_1, \ldots, u_n)$ and $v = (v_1, \ldots, v_n)$ in $\mathbf{F}_2^n$.

Definition 1.2. The *weight* $wt(u)$ of a vector $u \in \mathbf{F}_2^n$ is the number of non-zero entries in u.

$$C^\perp = \{v \in \mathbb{F}_2^n \mid v \cdot c = 0 \text{ for all } c \in C\}$$

Definition 1.3. A code $C \subseteq \mathbf{F}_2^n$ is a self-dual code of length n if $C = C^\perp$. It is said to be self-orthogonal if $C \subseteq C^\perp$.

Definition 1.4. A self-dual code is said to have *doubly-even weight* if its weight is congruent to 0 mod 4. A self-dual code where all vectors have doubly-even weight is said to be a *Type II code*.

Definition 1.5. A neighbor denoted by $N(C, \mathbf{v})$ can be constructed by

$$N(C, \mathbf{v}) = \langle \{\mathbf{w} \in C \mid [\mathbf{w}, \mathbf{v}] = 0\}, \mathbf{v} \rangle.$$

Alternatively, neighbor is defined as a code having a subcode of co-dimension 1 in common.

Theorem 1.6. *Let C be a self-dual code and let $\mathbf{v}$ be a self-orthogonal vector not in C. Then $N(C, \mathbf{v})$ is a self-dual code.*

Definition 1.7. An element of $\mathbf{F}_2^g$ is denoted by a column vector. For a code C, the weight enumerator of C in genus g is defined by

$$W_C^{(g)}(x_a : a \in \mathbb{F}_2^g) = \sum_{u_1, \ldots, u_g \in C} \prod_{a \in \mathbb{F}_2^g} x_a^{n_a(u_1, \ldots, u_g)}$$

where $n_a(u_1, \ldots, u_g) = \#\{i : a = (u_{1i}, u_{2i}, \ldots, u_{gi})\}$.

Definition 1.8. d_n^+ is a Type II code generated by the matrix:

$$\underbrace{\begin{bmatrix} 1 & 1 & 1 & 1 & \cdots & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & \cdots & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 & 1 & 1 & 1 \\ 1 & 0 & 1 & 0 & \cdots & 1 & 0 & 1 & 0 \end{bmatrix}}_{n}$$

There are 9 Type II codes of length 24 up to equivalence:

C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9
d_{12}^2	$d_{10}e_7^2$	d_8^3	d_6^4	d_{24}	d_6^4	g_{24}	$d_{16}e_8$	e_8^3

where C_1, C_5, C_8 are neighbors of d_{24}^+.

Theorem 1.9. *The invariant ring $\mathbb{C}[X_a]^{G_g}$ is generated by the weight enumerators of Type II codes in genus g.*

Proposition 1.10. *The dimension formulae of the invariant ring $\mathbb{C}[X_a]^{G_g}$ are:*

$$\frac{1}{(1-t^8)(1-t^{24})} = 1 + t^8 + t^{16} + 2t^{24} + \cdots, \quad \textit{for } g = 1,$$

$$\frac{1+t^{32}}{(1-t^8)(1-t^{24})^2(1-t^{40})} = 1 + t^8 + t^{16} + 3t^{24} + \cdots, \quad \textit{for } g = 2,$$

$$\frac{(1-t^4+t^8+\cdots+t^{24})(1+t^4)}{(1-t^8)(1-t^{16})(1-t^{24})^2\dots(1-t^{60})} = 1 + t^8 + 2t^{16} + 5t^{24} + \cdots, \quad \textit{for } g = 3.$$

2 Results

We use the following notations for various rings in genus g:

$\mathfrak{B}^{(g)}$	:	the ring of $W_C^{(g)}$, where C is a Type II code,
$\mathfrak{D}^{(g)}$	:	the ring of $W_{d_n^+}^{(g)}$, where $n \equiv 0 \pmod 8$,
$\mathfrak{A}^{(g)}$	:	the ring of $W_C^{(g)}$, where C is d_n^+ and its neighbors.

We propose the theorem of relation between $\mathfrak{B}^{(g)}$, $\mathfrak{D}^{(g)}$, $\mathfrak{A}^{(g)}$ in genus $1, 2, 3$.

Theorem 2.1. $\mathfrak{D}^{(1)} = \mathfrak{A}^{(1)} = \mathfrak{B}^{(1)}$ *up to the space of degree* 24.

Theorem 2.2. $\mathfrak{D}^{(2)} \subsetneq \mathfrak{A}^{(2)} = \mathfrak{B}^{(2)}$ *up to the space of degree* 24.

Theorem 2.3. $\mathfrak{D}^{(3)} \subsetneq \mathfrak{A}^{(3)} \subsetneq \mathfrak{B}^{(3)}$ *up to the space of degree* 24.

Remark 2.4. We took an example of d_n^+ of length 24. The weight enumerators for $g = 1$ case will be shown explicitly, while for $g = 2, 3$ will not due to the extensive length of the polynomials.

Proof. For $g = 1$, we know that C_5 is d_{24}^+ itself. Moreover, C_1, C_5 and C_8 are the neighbors of d_{24}^+. Since $W_{C_9}^{(1)}$ and $W_{C_5}^{(1)}$ are algebraically independent, therefore $\mathfrak{A}^{(1)} = \mathbb{C}[W_{e_8}^{(1)}, W_{d_{24}^+}^{(1)}] = \mathfrak{B}^{(1)}$.

For $g = 2$, we consider the genus 2 weight enumerators of e_8^3, d_{24}^+ and C_1. We select the following monomials of these weight enumerators:

$$\alpha x_{\substack{0\\0}}^{24}, \quad \beta x_{\substack{0\\0}}^{20} x_{\substack{0\\1}}^{4}, \quad \gamma x_{\substack{0\\0}}^{16} x_{\substack{0\\1}}^{8},$$

where $x_a \in \mathbb{F}_2^g$ and α, β and γ represent the coefficients of the monomials. Now we construct the following 3×3 matrix L which elements consist of the coefficients of the aforementioned 3 monomials from the selected weight enumerators:

Code	α	β	γ
e_8^3	1	42	591
d_{24}^+	1	66	495
C_1	1	30	639

Immediately, $\mathrm{Rank}(L) = 3$. It is known (by [6]) that the ring $\mathfrak{B}^{(2)}$ has the following structure:

$$\mathbb{C}[W_{e_8}^{(2)}, W_{d_{24}^+}^{(2)}, W_{g_{24}}^{(2)}, W_{d_{40}^+}^{(2)}] \oplus \mathbb{C}[W_{e_8}^{(2)}, W_{d_{24}^+}^{(2)}, W_{g_{24}}^{(2)}, W_{d_{40}^+}^{(2)}, W_{d_{32}^+}^{(2)}].$$

Since $\mathrm{Rank}(L) = 3$, the weight enumerators of e_8^3, d_{24}^+ and C_1 are algebraically independent. Thus the space of degree 24 in $\mathfrak{A}^{(2)}$ is of dimension 3 and is same as $\mathfrak{B}^{(2)}$.

To verify for the case $g = 3$, a matrix M is constructed with rows corresponding to the coefficients of the weight enumerators for the codes considered. We selected 4 monomials with $\alpha, \beta, \gamma, \delta$ being the coefficients of the aforementioned monomials. This is a 4×4 matrix representing 4 Type II codes and the coefficients of monomials in the weight enumerator polynomial:

Code	α	β	γ	δ
e_8^3	42	591	9491	592704
d_{24}^+	66	495	13860	110800
$d_{16}^+ \oplus e_8^+$	42	591	9492	762048
C_1	30	639	7020	659520

where the entries represent the coefficient of the selected monomials from each weight enumerator polynomials. It is immediate that $\mathrm{Rank}(M) = 4$. This means $W_{e_8^3}, W_{d_{24}^+}, W_{C_8}, W_{C_1}$ are algebraically independent and form a dimension 4 vector space. Thus the space of degree 24 in $\mathfrak{A}^{(3)}$ is of dimension 4 and hence it is strictly smaller than $\mathfrak{B}^{(3)}$. Moreover, the space of degree 24 in $\mathfrak{D}^{(3)}$ is of dimension 3. This completes the proof. □

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Computation of Vector-Valued Invariants for a Finite Complex Reflection Group

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Abstract. We consider the complex reflection group H_1, identified as No. 8 in the Shephard-Todd classification. In this presentation, we present computations of the vector-valued invariants associated with various representations of H_1. Additionally, we investigate the structure of the corresponding invariant rings.

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Centralizer Algebras of Two Permutation Groups of Order 1344

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There are two permutation groups that they share the same character table of order 1344. We take up natural representations on 8 and 14 letters respectively. The purpose of this paper is to examine the semi-simple structure of centralizing algebras in the tensor representation.

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First-principles study of ferroelectricity in $BaTiO_3$ thin-film

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Ferroelectricity is a very important component that can be applied in various applications. Even in the form of thin-film, this material is currently used in radio frequencies (RF) devices, nonvolatile memories, sensor and actuator applications, as well as microwave circuits that can be adjusted \cite{setter}. In this study, we attempted to understand the ferroelectric properties of $BaTiO_3$ thin-film using first-principles study. $BaTiO_3$, or Barium titanate, is one of the most basic and widely used ferroelectric oxide materials, with a perovskite crystal structure that has many excellent functional properties, such as dielectric, ferroelectric, piezoelectric, and electro-optic properties. Therefore, this material has been extensively used in various electronic devices. We have performed calculations using Density Functional Theory for bulk $BaTiO_3$ material (at room temperature ~27^{o}C) and obtained a double well potential indicating that the material is in a ferroelectric state. We have also performed the same calculations for $BaTiO_3$ in the form of a thin film (with a thickness of 1 u.c. - 5 u.c., at room temperature ~27^{o}C, assuming fabrication on a $SrTiO_3$ substrate), but so far we have not obtained a double well potential, meaning that the $BaTiO_3$ thin film at those thicknesses are in a paraelectric state. Some possible reasons for the absence of double well potential in a 1 u.c. - 5 u.c. thin-films are size limitations (1 u.c. - 5 u.c. thin film has a very small size, so its ferroelectric properties may differ from those of bulk material), surface effects (the surface of the thin-film can influence the ferroelectric properties of the material), so Double Well Potential may not be visible. Further research is recommended using much greater thin-film thicknesses, for example, thicknesses reaching 7 u.c. or even more.

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First-principles computational study on electronic structures in $Zn_2V_2O_7$ using quasi-particle self-consistent GW method

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Abstract:
In the recent decades, metal vanadate oxides have becomes the subject of research due its physical, photochemical and electrochemical properties. Zinc pyrovanadate is one of them and has a potential applications to the energy storage and other fields such as super-capacitor, lithium and aqueous zinc ion batteries, photoluminescence, and catalysis [1-3]. In the supercapacitor, the studied material shows a very high specific capacitance with storing charge in pseudo-capacitive way. In the aqueous zinc-ion batteries, the material displays synergistic effect with effective intercalation between its layers to store charge in batteries. Li^+, H^+ or Na^+ ions take part in the intercalation process. The bandgap favors applications in the photocatalytic water splitting. The studied material which is isostructural with $Cu_2P_2O_7$, belong to the thortveitite mineral ($Sc_2Si_2O_7$) group. The material shows phase transition under both temperature and pressure. Considering the temperature, the material shows a reversible second-order phase transition at 590°C [4]. The low-temperature phase or commonly known as α-phase crystallizes in monoclinic system with space group *C2/c*. while the high-temperature phase crystallizes in the same system as α-phase with *C2/m* space group. In our calculations, we used quasi-particle self-consistent GW (QSGW) method to investigate the electronic and optical properties of the structures in order to relate with the potential applications. We also calculate the structures utilizing density functional theory (DFT) for the comparison with QSGW method.

We report results computed with QSGW approach for the first time for the material under consideration, along with a comparison with DFT. The structural aspects for both phases are discussed at a greater length, mentioning the noticeable differences. Moving of bridging oxygen between V atoms to a higher symmetric and more hybridized position resulting in changing the space group from *C2/c* to *C2/m*. The total energies obtained from GGA-PBE shows more stability for low-temperature phase (α-phase) than for the high-temperature (β′-phase) phase which is consistent with experimental findings. The calculations of electronic band structure for the both phases indicates indirect semi-conducting nature with wide band gap value. The GGA-PBE computation provides underestimated band gap as usual while QSGW calculations largely overestimate. The band structure also reveals that the β′-phase is more disperse than the α phase, owing to the high symmetric position due to increasing temperature. The density of state calculations display the differences between the phases that arises from the structure. The crystal field effect (splitting of *d* orbital) is studied for *V-3d* orbital due to negative charges of tetrahedrally coordinated oxygen atoms. The optical absorption peaks arise from the transition between O-2p and V-3d orbital. The optical calculations suggest that overall, the material's sensitivity lies in the ultraviolet regions.

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Molecular Dynamics Simulations of Hemoglobin–Ligand Complexes for the Identification of Potential Anti-Polymerization Drug Candidates in Sickle Cell Disease

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This study aims to investigate the interaction between Compound 23 (ligand VUD) and the human hemoglobin receptor through an integrated computational approach combining molecular docking, molecular dynamics (MD) simulations, and binding free energy calculations using MM-PBSA (1–11). Molecular docking was first performed using AutoDock Vina, both with blind and targeted approaches, yielding binding affinities ranging from –7.6 to –8.3 kcal/mol, indicating favorable interactions between the ligand and multiple binding sites on the hemoglobin receptor. Subsequently, four systems were simulated for 100 ns using molecular dynamics: the hemoglobin complex with both ligands (chains A and C), the hipo (ligand-free) form, and systems containing only ligand A or ligand C. The RMSD and RMSF analyses showed that the complex with both ligands exhibited the most stable behavior, while the hipo form showed greater fluctuations. Notably, the chain C-bound system demonstrated higher stability than the chain A-bound system, supporting the notion that ligand binding to chain C contributes more significantly to complex stabilization. Binding free energy calculations using the MM-PBSA method further confirmed these results. The calculated ΔG_{bind} values were –34.98 kcal/mol (hipo), –9.70 kcal/mol (ligand C), and –12.09 kcal/mol (ligand A). Although the hipo form yielded the most favorable ΔG value due to system-specific energetic decomposition, both ligand-bound states demonstrated thermodynamically stable binding. These findings are consistent across structural and energetic analyses and strongly support the role of Compound 23 in stabilizing hemoglobin through specific chain interactions, particularly in chain C.

Keywords: compound 23, hemoglobin, sickle cell, molecular docking, molecular dynamics, binding free energy

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Rational Design of Quercetin Derivatives as Potent Breast Cancer Therapeutics: Insights from DFT, Docking, and Molecular Dynamics Approaches

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The conference was started from the cooperation between Bandung Institute of Technology, Indonesia and Kanazawa University, Japan in a series of meetings of scientists and graduate school students working in the domain of Computational Science in relation to Mathematics and Physics.

Cancer, especially breast cancer, remains a major health issue [1], with HER2 (Human Epidermal Growth Factor Receptor-2) overexpression observed in 20–30% of cases, leading to aggressive tumor growth and treatment resistance [2]. Quercetin, a flavonoid with known anticancer properties [3], was explored in this study through structural modification at positions 12, 15, and 16, introducing groups such as $–NO_2$, –CHO, –COMe, and $–SO_3H$. A total of 27 quercetin derivatives were designed and screened using molecular docking, dynamics, and pharmacokinetic (ADME-T) evaluations. Molecular docking simulations reveals that binding affinity scores of the tested ligands with HER2 range from -3.3 to -10.2 kcal/mol and its derivatives (1b, 2b, 3b, and 4b) demonstrated stronger binding affinities, attributed to the introduction of substituents at the 15^{th} position (<-9.3 kcal/mol). Based on ADME-T analysis, all quercetin derivatives, except for 4b which slightly exceeds the hydrogen bond donor limit, show good oral bioavailability (score: 0.55), along with favorable lipophilicity and solubility (logS ~ –3). None of the compounds are substrates of P-glycoprotein or able to cross the blood-brain barrier, reducing risks of efflux and CNS-related side effects, and 4b ligand has no interaction with CYP enzyme. Notably, compound 4b shows low plasma clearance, suggesting a longer systemic presence and the potential for less frequent dosing. Throughout the molecular dynamics simulation, the HER2–4b complex consistently maintained its hydrogen bonding interactions, indicating that ligand 4b stayed firmly positioned within the active site. The persistence of these interactions underscores the compound's capacity to uphold the structural stability of the complex over time, supporting its potential as a potent HER2 inhibitor. Additionally, the HER2–4b_3 complex displayed the lowest and most stable average radius of gyration (RoG) at 1.956 ± 0.014 nm, suggesting a compact and stable protein conformation was retained during the simulation. Binding free energy calculations (MM-PBSA/GBSA) confirmed 4b had the most negative ΔG_bind, indicating the strongest and most stable interaction. These results support 4b as a promising HER2-targeted anticancer agent.

Keywords: drug discovery, breast cancer, HER2, multiscale computational approaches

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First-Principles Investigation of Ferromagnetic Shape-Memory Materials via Quasiparticle Self-Consistent *GW* Approach

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Density functional theory (DFT), particularly with the local density approximation (LDA) and the generalized gradient approximation (GGA), is widely used for analysing and predicting physical properties. However, it often fails to accurately capture properties, such as band gaps, due to limitations of the DFT itself and the insufficient description of the exchange-correlation energy. To address such shortcomings, post-LDA methods such as LDA+U (with Hubbard corrections), hybrid functionals (with partial Fock exchange), and meta-GGA (including kinetic energy density), have been proposed. These techniques have demonstrated success in improving band gap predictions for semiconductor materials and are becoming de facto standards in DFT calculations. However, their performance in magnetic materials is more limited; for typical 3d ferromagnets, post-LDA methods tend to substantially overestimate magnetic moments and exchange interactions compared to experiment due to the excess electron localization [1]. As an alternative, many-body perturbation approaches such as the quasiparticle self-consistent GW (QSGW) method [2] incorporate electron correlation via the screened Coulomb interaction and provide more balanced treatments of quantum many-body effects. Notably, QSGW improves the overestimation issues observed in magnetic systems under post-DFT approaches [3].

In this study, we applied the QSGW method to investigate the ferromagnetic shape-memory alloys, specifically Ni-Mn-Ga (Heusler type) [4] and Fe-Pt ($L1_2$ type). Their shape-memory properties are attributed to martensitic transformations and long-period modulated structures, which result from their electronic structure. The magnetic moments obtained from QSGW calculations tend to slightly overestimate experimental values, yet they are closer to reality than those from other post-DFT methods. Furthermore, QSGW outperforms conventional GGA in reproducing the relative magnitudes of magnetic moments between austenite and martensite phases [5].

For the origin of the modulated structure, QSGW calculations revealed the electronic instability in the austenite phase through generalized susceptibility analysis on the high-temperature (austenite) phases, identifying a nesting vector corresponding to the 10M modulated structure [5,6]. Moreover, the direct calculation of the modulated structure, including 20 ~30 atoms in the unit cell, was performed thanks to the acceleration of QSGW calculation by GPU computing [7]. Notably, QSGW calculations reveal a dip in the minority-spin density of states near the Fermi level, a feature not captured by GGA, which is associated with the stabilization of the modulated magnetic phase.

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