

# Coarse-grained Interaction Potentials for Anisotropic Molecules

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We have proposed an efficient parameterization method for a recent variant of the Gay-Berne potential for dissimilar and biaxial particles and demonstrated it for a set of small organic molecules. Compared to the previously proposed coarse-grained models, the new potential exhibits a superior performance in close contact and large distant interactions. The repercussions of thermal vibrations and elasticity has been studied through a statistical method. The study justifies that the Potential of Mean Force is representable with the same functional form which extends the application of this coarse-grained description to a broader range of molecules. Moreover, the advantage of employing coarse-grained models instead of the well-known truncated atomistic summations with large distance cutoffs has been briefly studied for large molecules.

## I. INTRODUCTION

In molecular simulations, short-range attractive and repulsive interactions are typically represented using Lennard-Jones(6-12) potentials [1, 2]:

$$U_{LJ}(r; i, j) = 4\epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r} \right)^{12} - \left( \frac{\sigma_{ij}}{r} \right)^6 \right] \quad (1)$$

where  $\sigma_{ij}$  and  $\epsilon_{ij}$  are the effective heterogeneous interaction radius and well-depth between particles of type  $i$  and  $j$  respectively and  $r$  is the inter-particle displacement. While the  $r^{-6}$  part has a physical origin in dispersion or van der Waals interactions, the  $r^{-12}$  repulsion is chosen for mathematical convenience and is sometimes replaced by exponential terms as well. For large molecules, the exact evaluation of the interaction potential of this type involves a computationally expensive double summation over the respective (atomic) interaction sites:

$$U_{int}(\mathcal{M}_1, \mathcal{M}_2) = \sum_{i \in \mathcal{M}_1} \sum_{j \in \mathcal{M}_2} U_a(r_{ij}; i, j) \quad (2)$$

where  $\mathcal{M}_1$  and  $\mathcal{M}_2$  denote the interacting molecules and  $U_a(\cdot)$  is the atomic interaction potential, e.g. Eq. (1). In practice, a large distant interaction cutoff accompanied by a proper tapering is used to reduce the computation cost. More sophisticated and efficient summation methods such as Ewald summation and the Method of Lights are also widely used [3].

As an alternative approach, Gay and Berne [4] proposed a more complicated *single-site* interaction potential (in contrast to sophisticated summations) for uniaxial rigid molecules which was generalized to dissimilar and biaxial particles later by Berardi *et al* as well [5]. We will refer to this potential as the

biaxial-GB in the rest of this article. In response to the criticism of the unclear microscopic interpretation of the GB potential [6], we have recently used results from colloid science [7] to derive an approximate interaction potential based on the Hamaker theory [8] for mixtures of ellipsoids of arbitrary size and shape, namely the RE<sup>2</sup> potential [9]. Having a parameter space identical to that of Berardi, Fava and Zannoni [5], the RE<sup>2</sup> potential agrees significantly better with the numerically evaluated continuum approximation of Eq. (2), has no unphysical large distant limit and avoids the introduction of empirical adjustable parameters.

In an anisotropic coarse-grained model, a molecule  $\mathcal{M}$  is treated like a rigid body. Neglecting the atomic details, each molecule is characterized by a center separation  $\mathbf{r}$  and a transformation operator (a unitary matrix  $\mathbf{A}$  or a unit quaternion  $\mathbf{q}$ ) describing its orientation.

In the first section of the article, we briefly introduce the RE<sup>2</sup> potential followed by a review of the biaxial-GB potential and Buckingham(exp-6) atomistic model. The Buckingham(exp-6) potential is used in the MM3 force field [10] and will serve as the atomistic model potential for parameterizations. The second section describes a parameterization method which has been demonstrated for a few selected molecules, followed by an exemplar comparison between the RE<sup>2</sup> and the biaxial-GB potential will be presented. We will study the repercussion of internal vibrations (in contrast to the widely assumed proposition of the ideal stiffness) and propose an error analysis method to define trust temperature regions for single site potentials. Finally, we will show that the Potential of Mean Force (PMF) is representable with the same functional form for a wide range of temperatures.

## II. ATOMISTIC AND SINGLE-SITE NON-BONDED POTENTIALS

In the MM3 force field [10], the van der Waals interaction is described in terms of Buckingham(exp-6) potential

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which is an exponential repulsive accompanied by a  $r^{-6}$  attractive term:

$$U^{MM3}(r_{ij}; i, j) = \epsilon_{ij} \left( A e^{-B\sigma_{ij}/r_{ij}} - C \left( \frac{\sigma_{ij}}{r_{ij}} \right)^6 \right) \quad (3)$$

where A, B and C are fixed empirical constants while  $\sigma_{ij}$  and  $\epsilon_{ij}$  are heterogeneous interaction parameters specific to the interacting particles. Usually, Lorenz and Berthelot averaging rules are used to define heterogeneous interaction parameters in terms of the homogeneous ones, i.e.  $\sigma_{ij} = (\sigma_i + \sigma_j)/2$  and  $\epsilon_{ij} = \sqrt{\epsilon_i \epsilon_j}$ . The hard core repulsion is usually described via a  $r^{-12}$  term with an appropriate energy switching:

$$U_{HC}^{MM3}(r_{ij}; i, j) = \gamma \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} \quad (4)$$

where  $\gamma$  is defined in a way to provide continuity at the switching distance. The interaction energy between two arbitrary molecules is trivially the pairwise double summation over all of the interaction sites, i.e. Eq. (2).

The dissimilar and biaxial Gay-Berne potential (biaxial-GB) is a widely used single-site model proposed by Berardi et al. [5] which is an extension of the original uniaxial description [4] to biaxial molecules and heterogeneous interactions. Based on the original Gay and Berne concept, the biaxial-GB is a shifted Lennard-Jones(6-12) interaction between two biaxial Gaussian distribution of interacting sites. In this coarse-grained model, each molecule is described by two diagonal characteristic tensors (in the principal basis of the molecule)  $\mathbf{S}$  and  $\mathbf{E}$ , representing the half radii of the molecule and the strength of the pole contact interactions, respectively. As mentioned earlier, the orientation of a molecule is described by a center separation vector  $\mathbf{r}$  and a unitary operator  $\mathbf{A}$ , revolving the lab frame to the principal frame of the molecule.

The biaxial-GB description for the interaction between two molecules with a center separation of  $\mathbf{r}_{12} = \mathbf{r}_2 - \mathbf{r}_1$  and respective orientation tensors  $\mathbf{A}_1$  and  $\mathbf{A}_2$  is defined as:

$$U_{A,R}^{GB}(\mathbf{r}_{12}, \mathbf{A}_1, \mathbf{A}_2) = 4\epsilon_0 \eta_{12}^\nu \chi_{12}^\mu \left[ \left( \frac{\sigma_c}{h_{12} + \sigma_c} \right)^{12} - \left( \frac{\sigma_c}{h_{12} + \sigma_c} \right)^6 \right] \quad (5)$$

where  $\epsilon_0$  and  $\sigma_c$  are the energy and length scales,  $\eta_{12}$  and  $\chi_{12}$  are purely orientation dependant terms [5] and  $h_{12}$  is the the least contact distance between the two ellipsoids which are defined by the diagonal covariance tensor of the assumed Gaussian distributions. The orientation dependant terms ( $\eta_{12}$  and  $\chi_{12}$ ) describe the anisotropy of the molecules.

We have recently proposed a single-site potential, namely RE<sup>2</sup> [9] giving the approximate interaction energy between two hard ellipsoids in contrast to the

tradition of the Gaussian clouds, initiated by Gay and Berne [4]. The orientation dependence of the RE<sup>2</sup> potential fall at large distances, reducing asymptotically to the interaction energy of two spheres. Moreover, it gives a more realistic intermediate and close contact interaction using a heuristic interpolation of the Deryaguin expansion [9, 11]. Being a shifted Lennard-Jones(6-12) potential, the biaxial-GB fails to exhibit the correct functional behavior for large molecules [9]. The attractive and repulsive contributions of the RE<sup>2</sup> potential are respectively:

$$U_A^{RE^2}(\mathbf{A}_1, \mathbf{A}_2, \mathbf{r}_{12}) = -\frac{A_{12}}{36} \left( 1 + 3\eta_{12}\chi_{12} \frac{\sigma_c}{h_{12}} \right) \times \prod_{i=1}^2 \prod_{e=x,y,z} \left( \frac{\sigma_e^{(i)}}{\sigma_e^{(i)} + h_{12}/2} \right) \quad (6a)$$

$$U_R^{RE^2}(\mathbf{A}_1, \mathbf{A}_2, \mathbf{r}_{12}) = \frac{A_{12}}{2025} \left( \frac{\sigma_c}{h_{12}} \right)^6 \left( 1 + \frac{45}{56}\eta_{12}\chi_{12} \frac{\sigma_c}{h_{12}} \right) \times \prod_{i=1}^2 \prod_{e=x,y,z} \left( \frac{\sigma_e^{(i)}}{\sigma_e^{(i)} + h_{12}/60^{1/3}} \right) \quad (6b)$$

where  $A_{12}$  is the Hamaker constant (the energy scale),  $\sigma_c$  is the atomic interaction radius and  $\sigma_x^{(i)}$ ,  $\sigma_y^{(i)}$  and  $\sigma_z^{(i)}$  are the half-radii of  $i$ th ellipsoid ( $i=1,2$ ). The terms  $\eta_{12}$ ,  $\chi_{12}$  and  $h_{12}$  are defined in parallel to the biaxial-GB model and thus, are described in terms of the same characteristic tensors.

The structure tensor  $\mathbf{S}_i$  and the relative potential well depth tensor  $\mathbf{E}_i$  are diagonal in the principal basis of  $i$ th molecule and are defined as:

$$\mathbf{S}_i = \text{diag}\{\sigma_x^{(i)}, \sigma_y^{(i)}, \sigma_z^{(i)}\} \quad (7a)$$

$$\mathbf{E}_i = \text{diag}\{E_x^{(i)}, E_y^{(i)}, E_z^{(i)}\} \quad (7b)$$

where  $E_x^{(i)}$ ,  $E_y^{(i)}$  and  $E_z^{(i)}$  are dimensionless energy scales inversely proportional to the potential well depths of the respective orthogonal configurations of the interacting molecules ( $\mathbf{aa}$ ,  $\mathbf{bb}$  and  $\mathbf{cc}$ , Table I). For large molecules with uniform constructions, it has been shown [9] that the energy parameteres are approximately representable in terms of the local contact curvatures using the Deryaguin expansion [11]:

$$\mathbf{E}_i = \sigma_c \text{diag}\left\{ \frac{\sigma_x}{\sigma_y \sigma_z}, \frac{\sigma_y}{\sigma_x \sigma_z}, \frac{\sigma_z}{\sigma_x \sigma_y} \right\} \quad (8)$$

The assumptions leading to these estimations are not valid for the studied small organic molecules. Therefore, we will cease to impose further suppositions and take these three scales as independent characteristics of a biaxial molecule. Computable expressions for the orientation dependent factors of the RE<sup>2</sup> potential ( $\eta_{12}$  and  $\chi_{12}$ ) among with the Gay-Berne approximation for  $h_{12}$  has been given in the Appendix (A).

### III. PARAMETERIZATION FOR ARBITRARY MOLECULES

#### A. The Principal Basis and The Effective Center of Interaction

Associating a biaxial ellipsoid to an arbitrary molecule, one must define an appropriate principal basis and a center of interaction for it beforehand, according to the used coarse-grained model. Although there's no trivial solution to this problem, the centroid and the eigenbasis of the geometrical inertia tensor of the molecule are promising candidates and may be taken as suitable initial guesses as they yield to the correct solution at least for the molecules with perfect symmetry. For a molecule consisting of  $N$  particles, the centroid is defined as:

$$\mathbf{r}_c = \frac{\sum_{i=1}^N \mathbf{r}_i}{N} \quad (9)$$

and the principal basis is the eigenbasis of the geometrical inertia tensor  $\mathbf{I}_g$  given by:

$$\mathbf{I}_g = \sum_{i=1}^N (r_i^2 \mathbf{1} - \mathbf{r}_i \otimes \mathbf{r}_i) \quad (10)$$

where  $\mathbf{r}_i$  is the position of  $i$ th atom.

The most general parameter space of the RE<sup>2</sup> potential contains the energy and length scales, the characteristic tensors and the parameters specifying the relative orientation of the ellipsoids to the molecules. In order to overcome the degeneracy of the parameter space and to guarantee the rapid convergence of the optimization routines, a two-stage parameterization is proposed. In the first stage, the center and principal frame of the molecule will be fixed at the centroid and the eigenbasis of the inertia tensor. A preliminary optimization in the reduced parameter space yields to an approximate parameterization. In the second stage, the results of the first stage will be taken as the initial guess, followed by an optimization in the unconstrained variable space. This two-stage parameterization will theoretically result in superior results for molecules with imperfect symmetries.

#### B. Sampling and Optimization

Physical and symmetrical considerations lead to the proposition that a sampling of the pole contact interactions between two biaxial particles is essentially sufficient to reproduce the interaction for all configurations. There are 18 different orthogonal approaching configurations (pole contacts) between two dissimilar and biaxial particles (Table I). Based on physical grounds, we optimize the parameter space for the important characteristics of the sampled orthogonal energy profiles, i.e. potential well depth, potential well distance, the width of well

at half depth and the soft contact distance. This parameterization fashion is guaranteed to produce a satisfactory reconstruction of the most crucial region of interaction.

The geometry of the molecules were initially optimized using TINKER molecular modeling package [12] with the MM3 force field. We have used the same force field to sample the interaction energy for the orthogonal configurations.

Given a parameter tuple  $\mathbf{p}$ , we denote the potential well depth, well distance, well width at half depth and the soft contact distance for  $i$ th orthogonal configuration predicted by the RE<sup>2</sup> potential by  $U_m(i; \mathbf{p})$ ,  $R_m(i; \mathbf{p})$ ,  $W(i; \mathbf{p})$  and  $R_{sc}(i; \mathbf{p})$  respectively. The same potential well specifications calculated from the atomistic sum is denoted by scripted letters. An appropriate cost function is:

$$\Omega(\mathbf{p}) = \frac{1}{\Omega_0} \sum_{i=1}^{N_{\dagger}} e^{-\beta \mathcal{U}_m(i)} \left[ w_{U_m} \left( \frac{U_m(i; \mathbf{p}) - \mathcal{U}_m(i)}{\mathcal{U}_0} \right)^2 + w_{R_m} \left( \frac{R_m(i; \mathbf{p}) - \mathcal{R}_m(i)}{\mathcal{R}_0} \right)^2 + w_W \left( \frac{W(i; \mathbf{p}) - \mathcal{W}(i)}{\mathcal{W}_0} \right)^2 + w_{R_{sc}} \left( \frac{R_{sc}(i; \mathbf{p}) - \mathcal{R}_{sc}(i)}{\mathcal{R}_{sc0}} \right)^2 \right] \quad (11)$$

where  $\Omega_0$  is a normalization factor:

$$\Omega_0 = 4(w_{U_m}^2 + w_{R_m}^2 + w_W^2 + w_{R_{sc}}^2)^{\frac{1}{2}} \sum_{i=1}^{N_{\dagger}} e^{-\beta \mathcal{U}_m(i)}. \quad (12)$$

We have chosen  $\mathcal{U}_0$  as  $\min\{|\mathcal{U}_m(i)|\}$  and  $\mathcal{R}_0$ ,  $\mathcal{W}_0$  and  $\mathcal{R}_{sc0}$  as  $\min\{|\mathcal{W}_m(i)|\}$  based on physical considerations.  $N_{\dagger}$  is the number of orthogonal profiles (12 and 18 for homogeneous and heterogeneous interactions respectively) and  $(w_U, w_R, w_W, w_{R_{sc}})$  are fixed error partitioning factors for different terms, set to (1.0, 3.0, 2.5, 1.0) in order to emphasize on the structural details. We have also included a fixed error weighting according to the Boltzmann probability of the appearance of the corresponding profiles. One expects higher amplitude of relative appearance for orientations with deeper wells, which justifies the requisite of higher contribution in the cost function. We have also chosen  $\beta$  as  $1/\langle |\mathcal{U}_m(i)| \rangle$  in order to avoid deep submergence of the lower energy orientations.

Further implications such as matching the large distance behavior will be regarded as constraints on the parameter space, leaving the defined cost function unchanged.

The nonlinear optimization procedure consists of a preliminary Nelder-Mead Simplex search followed by a quasi-Newton search with BFGS Hessian updates [13].

The whole parameterization routine is coded in MATLAB/Octave and is freely available [14]. The procedures of sampling and parameterization are purely automated and requires only a Cartesian input file. The interaction parameters for the homogeneous interaction of a set of small prolate and oblate organic molecules has been provided in Table (II). It is noticed that the provided half radii agree significantly better with the molecular dimensions compared to the biaxial-GB parameterizations [5], reflecting the precise microscopic interpretation of the  $RE^2$  potential.

### C. Large Distance Analysis

The cost function defined in the previous section focuses on close contact regions only. In order to achieve the correct large distant limit as well, we will constrain the variable space by matching the asymptotic behavior of the  $RE^2$  potential with the atomistic summation. The asymptotic behavior of the  $RE^2$  potential is described as:

$$\lim_{r_{12} \rightarrow \infty} r_{12}^6 U_{RE^2}(\mathbf{r}_{12}, \mathbf{A}_1, \mathbf{A}_2) = -\frac{16}{9} A_{12} \det[\mathbf{S}_1] \det[\mathbf{S}_2] \quad (13)$$

The atomistic summation defined by Eq. (2) and Eq. (3) exhibits the same asymptotic behavior, which together with Eq. (13) results in the relation:

$$A_{12} \det[\mathbf{S}_1] \det[\mathbf{S}_2] = \frac{9}{16} \sum_{i \in A} \sum_{j \in B} \epsilon_{ij} \sigma_{ij}^6 \quad (14)$$

The summation appearing in right hand side is most easily evaluated by a direct force field parameter lookup. Applying such a constraint guarantees the expected large distant behavior while leads to a faster parameterization, reducing the dimensions of the variable space. Unconstrained optimization routines are still applicable as one may solve Eq. (14) for  $A_{12}$  explicitly. A graphical comparison between the biaxial-GB and the  $RE^2$  potential has been given for the homogeneous interaction of the pair Perylene [15] has been sketched in Fig. 1. The large distance convergence of the  $RE^2$  potential is noticed in contrast to the divergent behavior of the biaxial-GB potential, which is due to the non-vanishing orientation dependent pre-factors. Although the energy contribution is small at this limit, it is not generally negligible, e.g. the large distant separability of the orientation dependence of the model potential alters the nature of the phase diagram and the long range order of a hard rod fluid in general [16].

### D. Heterogeneous Interactions

The heterogeneous interaction between two molecules  $\mathcal{M}_1$  and  $\mathcal{M}_2$  is calculable by equations (6a) and (6b)

once the characteristic tensors of each molecule ( $\mathbf{S}$  and  $\mathbf{E}$ ) along with the heterogeneous Hamaker constant  $A_{\mathcal{M}_1\mathcal{M}_2}$  and the atomic potential radius  $\sigma_{\mathcal{M}_1\mathcal{M}_2}$  are available. The heterogeneous Hamaker constant may be evaluated directly with a force-field parameter lookup. Moreover, the arithmetic mean of  $\sigma_{\mathcal{M}_1\mathcal{M}_1}$  and  $\sigma_{\mathcal{M}_2\mathcal{M}_2}$  is a reasonable estimate for the heterogeneous interaction radius,  $\sigma_{\mathcal{M}_1\mathcal{M}_2}$ . Therefore, the homogeneous interaction parameters of the molecules  $\mathcal{M}_1$  and  $\mathcal{M}_2$  are sufficient to describe their respective heterogeneous interaction using the  $RE^2$  potential. Apparently, there is no trivial mixing rule available for the energy scale of the biaxial-GB potential. Inspired by the atomic mixing rules and the theory of the Gay-Berne potential, we have used Berthelot's geometric averaging rule for this purpose. An instance of a heterogeneous interaction has been illustrated in Fig. (2) for the pair Perylene (oblate) and Sexithiophene (prolate) [15]. The results are quite promising for a coarse-grained model; However, further optimization will theoretically yield to superior results. Concluding from the graphs, the  $RE^2$  potential performs significantly better at end-to-end and cross interactions compared to the biaxial-GB. The error measures ( $\Omega_{RE^2} = 6.5 \times 10^{-3}$ ,  $\Omega_{GB} = 7.7 \times 10^{-3}$ ) agree with this observation.

### E. The advantages over practical atomistic implementations

As mentioned before, the atomistic evaluation of long-range interaction potentials involve computationally expensive double summations over the interaction sites, resulting in a quadratic time cost with respect to the average number of interactions sites. However, the average computation time of a single-site potential is intrinsically constant, regardless of the number of interacting atoms. These observations have been quantified in Fig. (3) which is a comparison between the computation time of an exact LJ(6-12) atomistic summation and an efficient implementation of the  $RE^2$  potential [14]. Concluding from the graph, employing the  $RE^2$  potential for molecules consisting as low as  $\sim 5$  atoms (or  $\sim 25$  overall atomic interactions) is economic.

The atomistic summations are practically employed with a proper large distance cutoff in order to reduce the computation time. Considerable errors may be introduced by choosing small cutoff distances compared to the dimensions of the interacting molecules. Therefore, it is expectable that a coarse-grained model yield to relatively better results compared to the truncated atomistic summations in certain configurations. A figurative situation is the end-to-end interaction of two prolate molecules, illustrated in Fig. (4) for Pentacene molecule [15]. The first panel of Fig. (4) is a semi-log plot of the relative error for the  $RE^2$  potential accompanied by three atomistic approximations with different cutoffs (6, 9 and 12

Å). The discontinuity of the truncated atomistic summations is a result of hard cutoffs. Concluding from the graphs, the coarse-grained description introduces less error in all ranges of this configuration while requires a considerably lower computation time.

#### IV. INTERMOLECULAR VIBRATIONS AND SINGLE-SITE POTENTIALS

In this section, we study the proposition of ideal rigidity of the molecules, which is widely assumed in single-site approximations of extended molecules, including our own study in the previous sections. The samplings are usually taken from the relative orientations of the unperturbed and geometrically optimized structures. The resulting parameterization will be used in molecular dynamics simulations in which internal vibrations may not be negligible. We will introduce a method to estimate the error introduced by this supposition in the first part of this study. A parameterization based on the Potential of Mean Force (PMF) is probably the best one can achieve with the coarse-grained models, although the samplings are expensive. We will study such parameterizations in the second part.

##### A. Analysis of the Mean Relative Error

The PMF for the interaction of semi-rigid molecules in an arbitrary ensemble may be expressed as an additive correction term to the the interaction potential of the respective rigid molecules. We will show that these correction terms are expressible in terms of statistical geometric properties of a molecule in the ensemble. The PMF between two molecules  $\mathcal{M}_1$  and  $\mathcal{M}_2$  with a mean center separation of  $\mathbf{r}_{12} = \mathbf{r}_2 - \mathbf{r}_1$  and mean orientation tensors  $\mathbf{A}_1$  and  $\mathbf{A}_2$  is defined as:

$$U_{pmf}(\mathbf{r}_{12}, \mathbf{A}_1, \mathbf{A}_2) = \langle U(\mathcal{M}_1, \mathcal{M}_2) \rangle \quad (15)$$

where  $\langle \cdot \rangle$  denotes the ensemble averaging. The mean location of intermolecular particles are expected to remain unchanged compared to the unperturbed structures for a large range of temperatures as the internal structures of semi-rigid molecules are mainly governed by harmonic bond stretching and angle bending potentials.

We may assume the location of each particle as a random variable, sharply peaked at its mean value. Therefore, we denote the location of  $i$ th particle measured in its principal coordinate system by:

$$\mathbf{r}_i = \bar{\mathbf{r}}_i + \delta\mathbf{r}_i \quad (16)$$

where  $\bar{\mathbf{r}}_i = \langle \mathbf{r}_i \rangle$  and  $\delta\mathbf{r}_i$  is a displacement due to internal vibrations with vanishing average. The PMF of the interaction between the molecules  $\mathcal{M}_1$  and  $\mathcal{M}_2$  is defined

as:

$$U_{pmf}(\mathbf{r}_{12}, \mathbf{A}_1, \mathbf{A}_2) = \left\langle \sum_{i \in \mathcal{M}_1} \sum_{j \in \mathcal{M}_2} U_a(\|\mathbf{r}_i - \mathbf{r}_j\|; i, j) \right\rangle \quad (17)$$

where  $U_a(\cdot)$  is the atomistic interaction potential. It is easy to show that up to the second moments:

$$\langle \|\mathbf{r}_i - \mathbf{r}_j\| \rangle \simeq \|\mathbf{r}_{ij}^0\| + \frac{1}{2\|\mathbf{r}_{ij}^0\|} \sum_{k=3}^3 \text{Var}(\delta\mathbf{r}_i - \delta\mathbf{r}_j) \cdot \hat{\mathbf{e}}_k \left( 1 - \frac{(\mathbf{r}_{ij}^0 \cdot \mathbf{e}_k)^2}{\|\mathbf{r}_{ij}^0\|^2} \right) \quad (18)$$

where  $\mathbf{r}_{ij}^0 = \bar{\mathbf{r}}_i - \bar{\mathbf{r}}_j$ . We have neglected the covariance between the coordinates. Using the last relation, we reach to a second-order estimate of Eq. (17):

$$\begin{aligned} U_{pmf}(\mathbf{r}_{12}, \mathbf{A}_1, \mathbf{A}_2; \mathcal{M}_1, \mathcal{M}_2) \simeq & \sum_{i \in \mathcal{M}_1} \sum_{j \in \mathcal{M}_2} U_a(\|\bar{\mathbf{r}}_i - \bar{\mathbf{r}}_j\|; i, j) + \\ & \frac{1}{2} \sum_{i \in \mathcal{M}_1} \sum_{j \in \mathcal{M}_2} \left( \sum_{k=1}^3 \text{Var}(\delta\mathbf{r}_i - \delta\mathbf{r}_j) \cdot \hat{\mathbf{e}}_k \times \right. \\ & \left. \left( 1 - \frac{(\mathbf{r}_{ij}^0 \cdot \mathbf{e}_k)^2}{\|\mathbf{r}_{ij}^0\|^2} \right) \frac{U'_a(\|\mathbf{r}_{ij}^0\|; i, j)}{\|\mathbf{r}_{ij}^0\|} + \right. \\ & \left. \sum_{k=1}^3 \text{Var}(\delta\mathbf{r}_i - \delta\mathbf{r}_j) \cdot \hat{\mathbf{e}}_k \frac{(\mathbf{r}_{ij}^0 \cdot \mathbf{e}_k)^2}{\|\mathbf{r}_{ij}^0\|^2} U''_a(\|\mathbf{r}_{ij}^0\|; i, j) \right) \quad (19) \end{aligned}$$

The first term of the right hand side is the interaction energy of the averaged structures, where the remaining terms are second-order corrections. The RMS of the relative error introduced by neglecting the correction terms (e.g. the error in parameterizations based on unperturbed samplings) may be evaluated formally via the following integral:

$$\mathcal{E}(T) = \left( \frac{1}{\mathcal{E}_0(T)} \int_{\omega \in \Omega(T)} \exp\left(-\frac{U(\omega)}{k_B T}\right) \left[ \frac{\delta U(\omega)}{U(\omega)} \right]^2 dN_\omega \right)^{\frac{1}{2}} \quad (20)$$

where  $\omega$  is a relative orientation,  $dN_\omega$  is a differential measure of orientations near  $\omega$ ,  $\Omega(T)$  being the ensemble and  $\delta U(\omega)$  is the second-order correction defined by Eq. (19).  $\mathcal{E}_0(T)$  is the normalization factor defined as:

$$\mathcal{E}_0(T) = \int_{\omega \in \Omega(T)} \exp\left(-\frac{U(\omega)}{k_B T}\right) dN_\omega \quad (21)$$

In practice, the spatial variance of each particle in an ensemble is most easily obtainable through an MD simulation. Once the statistical information are accessible,  $\mathcal{E}(T)$  is most easily evaluated by Monte Carlo integration. Neglecting the covariance between the dislocation of the particles, we are implicitly overlooking the stretching and bending of the molecules at close contact configurations. Although our proposed error

analysis disregards this phenomenon, it still measures the introduced error due to purely thermal vibrations.

We have demonstrated this error analysis method for three different molecules in a large range of temperatures. The statistical information was extracted from several MD simulation snapshots with the aid of TINKER molecular modeling package [12], each with 32 molecules and with periodic boundary conditions in an NVT ensemble (Fig. 5). For each isothermal ensemble, the RMS error has been evaluated using the MC integration of Eq. (20) for  $10^5$  random orientations. The relation between the RMS error and the temperature is noticeably linear. The linear regression analysis has been given at Table (III). According to the required degree of precision, one can define a trust region for the temperature using diagrams like Fig. (5). For example, a mean relative error of less than 10% is expected for temperatures less than 1500K in a homogeneous ensemble of Benzene molecules, concluding from the graph. It is also concluded that the studied prolate molecule (Sexithiophene) exhibits a higher relative error due to its considerably higher elasticity, compared to the oblate molecules (Perylene and Benzene).

### B. Parameterizations based on the Potential of Mean Force

The error introduced by the assumption of ideal rigidity may not be negligible for certain purposes, concluding from the previous analysis. However, a coarse-grained potential which is parameterized on a PMF basis is theoretically advantageous as it is expected to describe the mean behaviors closer to the atomistic model. Phenomenologically speaking, the internal degrees of freedom will soften the repulsions at close contacts while the thermal vibrations are expected to smoothen the orientation and separation dependencies of the interaction.

The PMF for a given macroscopic orientation may be evaluated through a Constrained Molecular Dynamics simulation (CMD) process with appropriate restrains. We have used harmonic restraining potentials for the center separation vector and on the deviations from the desirable principal basis for each molecule in order to keep them at the desired orientation. In order to reduce the random noise of the evaluated PMF, we applied a fifth-order Savitsky-Golay smoothing filter followed by a piecewise cubic Hermite interpolating polynomial fitting to the PMF samples.

Fig. (6) is a plot of the evaluated PMF between the pair perylene for the cross configuration **bc**. The upper (and interior) plots refer to higher temperatures. The expansion of the potential well width at lower temperatures is related to the tendency of the molecules to bend and stretch and thus, resulting in a softer interaction

while the shift of the soft contact and potential well distance along with the elevation of the potential well is associated to the thermal vibrations and hence, the expansion of the effective volume of the molecules. The temperature-dependant parameterizations (based on the evaluated PMF) given at Table (IV) justifies these qualitative discussions. One may associate the contraction of the molecule ( $\sigma_x$ ,  $\sigma_y$  and  $\sigma_z$ ) and the expansion of the atomic interaction radius at lower temperatures to contraction of the molecule at rough repulsions and widening of the potential well, respectively. Furthermore, the expansion of the molecule volume at higher temperatures reflect the overcoming of thermal vibrations to the flexibility of the molecule. According to tables (II) and (IV), the overall error measures ( $\Omega$ ) for PMF parameterizations closely match the same measure for the unperturbed structure. Thus, the same functional form may be used to represent the PMF as well.

## V. CONCLUSION

We have proposed and demonstrated a parameterization method for the RE<sup>2</sup> anisotropic single-site interaction potential which leads to a globally valid description of the attractive and repulsive interaction between arbitrary molecules. Unlike the biaxial-GB [5], the RE<sup>2</sup> potential gives the correct large distant interaction (Fig. 1) while having a superior performance in the close contact region (Fig. 2). The Potential of Mean Force is representable with the same functional form of the RE<sup>2</sup> potential. Compared to the parameterizations given at [5], The structure tensors agree significantly better with the spatial distribution of the intermolecular particles. It has also been shown that the coarse-gained models perform significantly better at certain configurations in comparison to a truncated atomistic summation with large distance cutoffs.

## VI. ACKNOWLEDGMENT

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## APPENDIX A: THE ORIENTATION DEPENDENT TERMS

We will briefly quote computable expressions for the orientation dependant terms from the original article [9]. The term  $\chi_{12}$  quantifies the strength of interaction with respect to the local atomic interaction strength of the molecules and is defined as:

$$\chi_{12}(\mathbf{A}_1, \mathbf{A}_2, \hat{\mathbf{r}}_{12}) = 2\hat{\mathbf{r}}_{12}^T \mathbf{B}_{12}^{-1}(\mathbf{A}_1, \mathbf{A}_2) \hat{\mathbf{r}}_{12} \quad (\text{A1})$$

where  $\mathbf{B}_{12}$  is defined in terms of the orientation tensors  $\mathbf{A}_i$  and relative well-depth tensors  $\mathbf{E}_i$ :

$$\mathbf{B}_{12}(\mathbf{A}_1, \mathbf{A}_2) = \mathbf{A}_1^T \mathbf{E}_1 \mathbf{A}_1 + \mathbf{A}_2^T \mathbf{E}_2 \mathbf{A}_2. \quad (\text{A2})$$

The term  $\eta_{12}$  describes the effect of contact curvatures of the molecules in the strength of the interaction and is defined as:

$$\eta_{12}(\mathbf{A}_1, \mathbf{A}_2, \hat{\mathbf{r}}_{12}) = \frac{\det[\mathbf{S}_1]/\sigma_1^2 + \det[\mathbf{S}_2]/\sigma_2^2}{[\det[\mathbf{H}_{12}]/(\sigma_1 + \sigma_2)]^{1/2}}, \quad (\text{A3})$$

The projected radius of  $i$ th ellipsoid along  $\hat{\mathbf{r}}_{12}$  ( $\sigma_i$ ) and the tensor  $\mathbf{H}_{12}$  are defined respectively as:

$$\sigma_i(\mathbf{A}_i, \hat{\mathbf{r}}_{12}) = (\hat{\mathbf{r}}_{12}^T \mathbf{A}_i^T \mathbf{S}_i^{-2} \mathbf{A}_i \hat{\mathbf{r}}_{12})^{-1/2} \quad (\text{A4})$$

$$\mathbf{H}_{12}(\mathbf{A}_1, \mathbf{A}_2, \hat{\mathbf{r}}_{12}) = \frac{1}{\sigma_1} \mathbf{A}_1^T \mathbf{S}_1^2 \mathbf{A}_1 + \frac{1}{\sigma_2} \mathbf{A}_2^T \mathbf{S}_2^2 \mathbf{A}_2. \quad (\text{A5})$$

There's no general solution to the least contact distance between two arbitrary ellipsoids ( $h_{12}$ ). The Gay-Berne approximation [4, 6] is usually employed due to its low complexity and promising performance:

$$h_{12}^{GB} = \|\mathbf{r}_{12}\| - \sigma_{12} \quad (\text{A6})$$

The anisotropic distance function  $\sigma_{12}$  [5] is defined as:

$$\sigma_{12} = \left( \frac{1}{2} \hat{\mathbf{r}}_{12}^T \mathbf{G}_{12}^{-1} \hat{\mathbf{r}}_{12} \right)^{-\frac{1}{2}} \quad (\text{A7})$$

where the symmetric overlap tensor  $\mathbf{G}_{12}$  is:

$$\mathbf{G}_{12} = \mathbf{A}_1^T \mathbf{S}_1^2 \mathbf{A}_1 + \mathbf{A}_2^T \mathbf{S}_2^2 \mathbf{A}_2 \quad (\text{A8})$$

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- [1] M.P. Allen and D.J. Tildesley. *Computer Simulation of Liquids*. Oxford University Press, Oxford, 1989.
- [2] D. Frenkel and B. Smit. *Understanding Molecular Simulations*. Academic Press, New York, 2002.
- [3] Andrew R. Leach. *Molecular Modelling: Principles and Applications*. Addison Wesley Longman Limited, 1996.
- [4] J. G. Gay and B. J. Berne. *J. Chem. Phys.*, 74(3316), 1981.
- [5] C. Fava R. Berardi and C. Zannoni. A gay-berne potential for dissimilar biaxial particles. *Chem. Phys. Lett.*, 297:8–14, 1998.
- [6] E. Praestgaard J. L. Lobowitz J. W. Perram, J. Rasmussen. *Phys. Rev. E*, 54(6565), 1996.
- [7] R. J. Hunter. *Foundations of Colloid Science*. Oxford University Press, Oxford, 2001.
- [8] H. C. Hamaker. *Physica*, 4(1058), 1937.
- [9] R. Everaers and M. R. Ejtehadi. Interaction potentials for soft and hard ellipsoids. *Physical Review E*, 67(041710), 2003.
- [10] J.-H. Lii and N. L. Allinger. Molecular mechanics. the mm3 force field for hydrocarbons. 3. the van der waals' potentials and crystal data for aliphatic and aromatic hydrocarbons. *J. Am. Chem. Soc.*, 111:8576–8582, 1989.
- [11] B. V. Deryaguin. *Kolloid Z.*, 69(155), 1934.
- [12] J. W. Ponder. *TINKER software tools for molecular design (V4.2) user's guide*, June 2004. freely available through <http://dasher.wustl.edu/tinker/>.
- [13] Stephen J. Wright Jorge Nocedal. *Numerical Optimization*. Springer Series in Operations Research. Springer-Verlag, New York, 1999.
- [14] The parameterization routine (MATLAB/Octave) among with an efficient set of C subroutines for the evaluation of  $RE^2$  interaction potential and its analytic derivatives is freely available at <http://mehr.sharif.edu/~softmatter/REsquare/>.
- [15] The chemical formula for the studied molecules are: (1) Perylene [ $C_{20}H_{12}$ ] (2) Pyrene [ $C_{16}H_{10}$ ] (3) Coronene [ $C_{24}H_{12}$ ] (4) Benzene [ $C_6H_8$ ] (5) Sexithiophene [ $S_6C_{24}H_{14}$ ] (6) Pentacene [ $C_{20}H_{16}$ ] (7) Anthracene [ $C_{14}H_{10}$ ] (8) Naphthalene [ $C_{10}H_8$ ] (9) Toluene [ $C_7H_8$ ].
- [16] D. Frenkel J. A. Cuesta. *Phys. Rev. A*, 42(2126), 1990.

TABLE I: The 18 orthogonal configurations of two dissimilar biaxial particles. A unitary operator ( $\mathbf{U}$ ) followed by a translation is applied to the second particle to reach the desired configuration. We adopt the naming scheme introduced by Berardi *et al* [5]. The operator  $\mathbf{R}_e$  denotes a  $\pi/2$  rotation with respect to the axis  $e$ . A two-letter code is attached to each configuration with respect to the faces perpendicular to connecting vector of the ellipsoids. A prime is added if one or three axes are antiparallel. Italic codes refer to configurations which are degenerate in homogeneous interactions.

$\mathbf{U}$	$\mathbf{r}_{12} \parallel \hat{\mathbf{e}}_{x1}$	$\mathbf{r}_{12} \parallel \hat{\mathbf{e}}_{y1}$	$\mathbf{r}_{12} \parallel \hat{\mathbf{e}}_{z1}$
$\mathbf{I}$	aa	bb	cc
$\mathbf{R}_z$	ab	<i>ba'</i>	<i>cc'</i>
$\mathbf{R}_y$	<i>ac'</i>	<i>bb'</i>	<i>ca'</i>
$\mathbf{R}_x \mathbf{R}_y$	<i>ac</i>	<i>ba</i>	<i>cb</i>
$\mathbf{R}_z \mathbf{R}_x \mathbf{R}_y$	<i>aa'</i>	<i>bc'</i>	<i>cb'</i>
$\mathbf{R}_x^T \mathbf{R}_z^T$	ab	bc	ca

TABLE II:  $\text{RE}^2$  potential parameters for homogeneous interactions of selected molecules [15]. The oblate molecules are: (1) Perylene (2) Pyrene (3) Coronene (4) Benzene. The prolate molecules are: (5) Sexithiophene (6) Pentacene (7) Anthracene (8) Naphthalene (9) Toluene.

Mol. No.	$A_{12}(10^2 \text{ Kcal/mol})$	$\sigma_c(\text{\AA})$	$\sigma_x(\text{\AA})$	$\sigma_y(\text{\AA})$	$\sigma_z(\text{\AA})$	$E_x$	$E_y$	$E_z$	$\Omega(10^{-3})$
Oblate:									
(1)	36.36	3.90	4.20	3.12	0.49	3.96	2.39	0.49	9.6
(2)	28.36	3.91	4.24	3.07	0.45	3.98	2.35	0.43	9.9
(3)	21.01	3.83	4.27	4.26	0.54	2.84	2.85	0.35	12.5
(4)	84.95	3.99	2.14	1.82	0.36	4.60	3.70	1.03	6.8
Prolate:									
(5)	49.44	4.07	10.96	1.99	0.46	6.30	1.16	0.35	10.7
(6)	37.46	3.88	6.56	2.28	0.47	5.52	1.65	0.43	9.7
(7)	45.51	3.85	4.19	2.25	0.44	6.83	2.48	0.62	9.2
(8)	37.76	3.82	3.09	2.20	0.49	4.59	3.39	0.77	10.9
(9)	23.19	3.75	2.72	2.04	0.57	4.61	3.29	1.00	10.6

TABLE III: Linear regression analysis between  $(\delta U/U)_{RMS}$  and T for a few selected molecules [15]. The molecules are: (1) Benzene (2) Perylene (3) Sexithiophene. The linear relationship is defined as  $(\delta U/U)_{RMS} = AT+B$  in all cases.

Mol. No.	$A(10^{-4} K^{-1})$	$B(10^{-3})$	$R^2$
(1)	0.66	1.0	0.987
(2)	1.39	-4.1	0.983
(3)	2.35	1.3	0.995

TABLE IV:  $\text{RE}^2$  potential parameters for the homogeneous interactions of the pair perylene at different temperatures.

Temperature (K)	$A_{12}(10^4 \text{ Kcal/mol})$	$\sigma_c(\text{\AA})$	$\sigma_x(\text{\AA})$	$\sigma_y(\text{\AA})$	$\sigma_z(\text{\AA})$	$E_x$	$E_y$	$E_z$	$\Omega(10^{-3})$
100	14.59	4.83	3.77	2.69	0.10	3.56	2.13	0.41	15.2
300	2.04	4.51	3.97	2.85	0.24	3.52	2.18	0.43	14.1
500	1.21	4.40	4.04	2.91	0.30	3.49	2.20	0.44	12.6
700	0.99	4.33	4.09	2.97	0.32	3.53	2.19	0.44	12.4
900	0.82	4.31	4.09	2.98	0.35	3.43	2.15	0.44	12.6

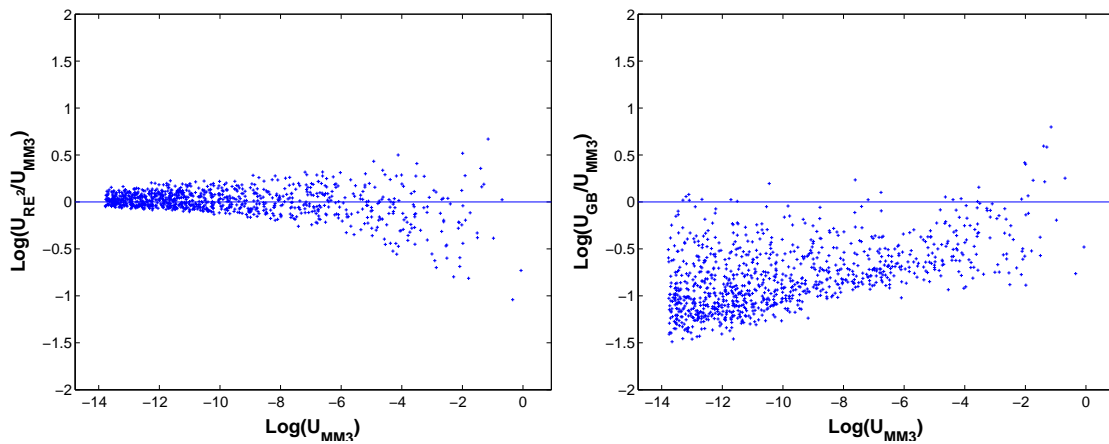


FIG. 1: A comparison between the  $RE^2$  and biaxial-GB potentials for the homogeneous interaction of the pair perylene in a set of uniform random center separations in the range  $[5\text{\AA}, 50\text{\AA}]$  along with random rotations. The Gay-Berne approximation has been used for the least contact distance. (a) A log-log plot of  $U_{RE^2}/U_{MM3}$  against  $U_{MM3}$  (Mean=-0.002, SD=0.08) (b) A log-log plot of  $U_{GB}/U_{MM3}$  against  $U_{MM3}$  (Mean=-0.87, SD=0.54)

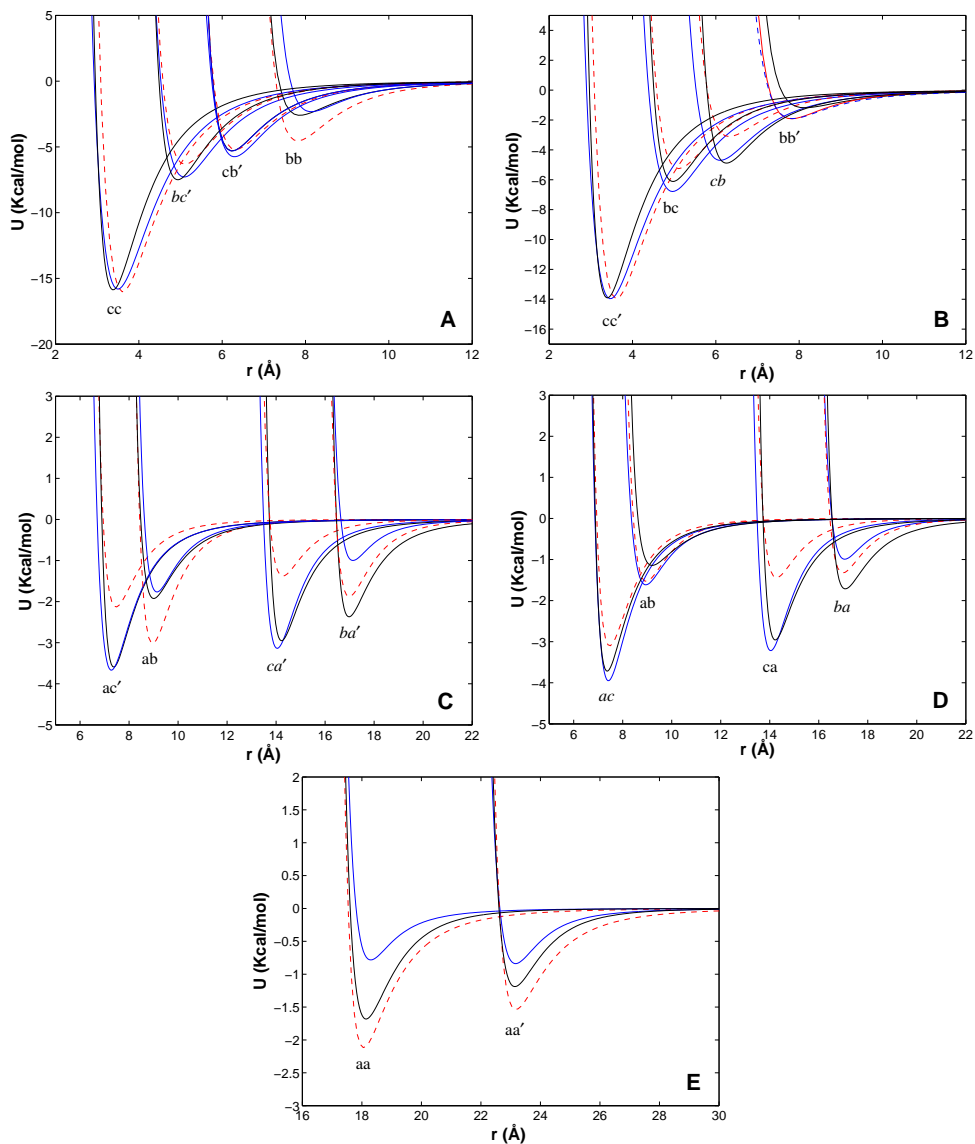


FIG. 2: The heterogeneous interaction between the pair perylene (oblate) and sextiophene (prolate) for the 18 orthogonal configurations. The black thick lines denote the  $RE^2$  potential, the red dashed lines refer to the biaxial-GB [5] and the reference atomistic summation (MM3 [10]) is denoted by blue thin lines. A combination of homogeneous interaction parameters (Table II) have been used without further optimization. The error measures are:  $\Omega_{RE^2} = 6.5 \times 10^{-3}$ ,  $\Omega_{GB} = 7.7 \times 10^{-3}$ . The graphs are grouped in five plates as: side-by-side (A), cross (B), T-shaped 1 (C), T-shaped 2 (D) and end-to-end (E) interactions and are labeled according to the notation introduced in Table (I).

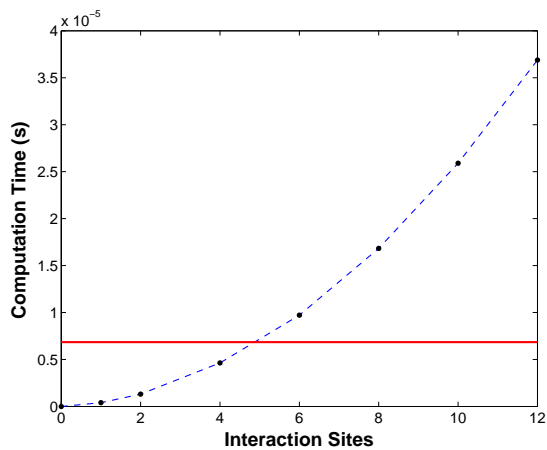


FIG. 3: The average computation time of exact LJ(6-12) atomistic summation with respect to the average number of interacting sites (blue dashed line) and  $RE^2$  single-site potential (red continuous line).

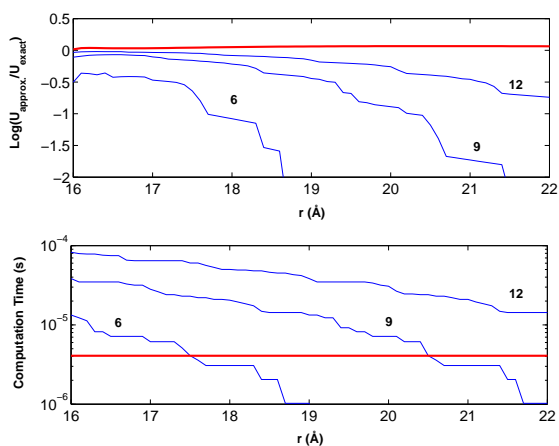


FIG. 4: A comparison between the approximate atomistic descriptions with hard cutoffs and the  $RE^2$  potential for the end-to-end interaction of the pair Pentacene. Thick lines denote the  $RE^2$  potential while thin lines represent atomistic summations with different cutoffs (6, 9 and 12 Å). (A) Logarithmic relative error of the  $RE^2$  potential and truncated atomistic summations to the exact atomistic summations vs. center separation. (B) Time consumption of different approximations vs. center separation.

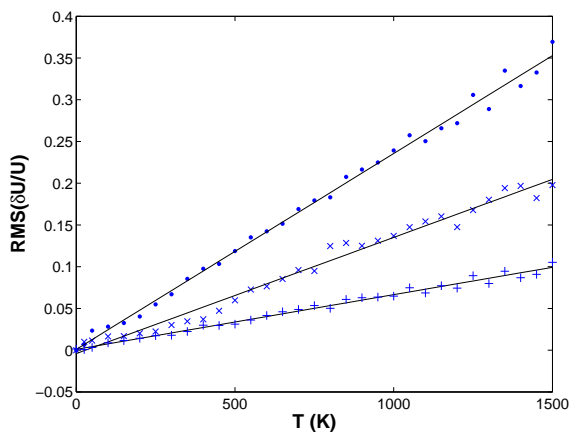


FIG. 5: Relative deviations from the PMF vs. temperature for three different molecules. The signs indicate the MD simulation data. The continuous lines are linear regressions. (1) Plus signs: Benzene (2) Cross signs: Perylene (3) Dots: Sexithiophene.

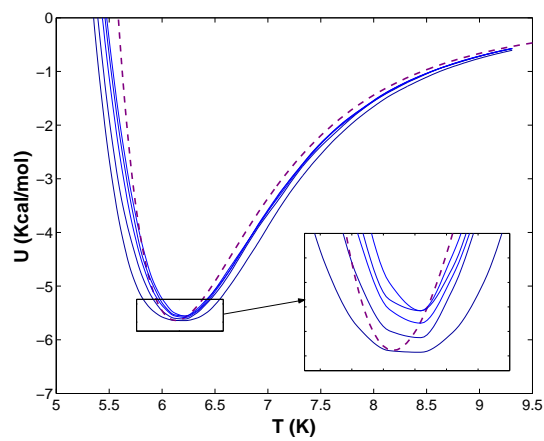


FIG. 6: Potential of Mean Force between the pair perylene for the cross configuration **bc**. The dashed line indicate the interaction potential of the unperturbed structures while the continuous lines, ordered descending with respect to their well-depths, represent the PMF at temperatures 100K, 300K, 500K, 700K and 900K, respectively.