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# Analysis of the conformational dependence of mass-metric tensor determinants in serial polymers with constraints

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It is well known that mass-metric tensor determinants $\det(\mathbf{G}_s)$ influence the equilibrium statistics and the rates of conformational transitions for polymers with constrained bond lengths and bond angles. It is now standard practice to include a Fixman-style compensating potential of the form $U_c(\mathbf{q}_s)\propto(-k_BT/2)\ln[\det(\mathbf{G}_s)]$ as part of algorithms for torsional space molecular dynamics. This elegant strategy helps eliminate unwarranted biases that arise due to the imposition of holonomic constraints. However, the precise nature and extent of variation of $\det(\mathbf{G}_s)$ and hence $\ln[\det(\mathbf{G}_s)]$ with chain conformation and chain length has never been quantified. This type of analysis is crucial for understanding the nature of the conformational bias that the introduction of a Fixman potential aims to eliminate. Additionally, a detailed analysis of the conformational dependence of $\det(\mathbf{G}_s)$ will help resolve ambiguities regarding suggestions for incorporating terms related to $\det(\mathbf{G}_s)$ in the design of move sets in torsional space Monte Carlo simulations. In this work, we present results from a systematic study of the variation of $\det(\mathbf{G}_s)$ for a serial polymer with fixed bond lengths and bond angles as a function of chain conformation and chain length. This analysis requires an algorithm designed for rapid computation of $\det(\mathbf{G}_s)$ which simultaneously allows for a physical/geometric interpretation of the conformational dependence of $\det(\mathbf{G}_s)$. Consequently, we provide a detailed discussion of our adaptation of an $O(n)$ algorithm from the robotics literature, which leads to simple recursion relations for direct evaluation of $\det(\mathbf{G}_s)$. Our analysis of the conformational dependence of $\det(\mathbf{G}_s)$ yields the following insights. (1) $\det(\mathbf{G}_s)$ is maximized for spatial conformers and minimized for planar conformations. (2) Previous work suggests that it is logical to expect that the conformational dependence of $\det(\mathbf{G}_s)$ becomes more pronounced with increase in chain length. Confirming this expectation, we provide systematic quantification of the nature of this dependency and show that the difference in $\det(\mathbf{G}_s)$ between spatial and planar conformers, i.e., between the maxima and minima of $\det(\mathbf{G}_s)$ grows systematically with chain length. Finally, we provide a brief discussion of implications of our analysis for the design of move sets in Monte Carlo simulations. [DOI: 10.1063/1.1821492]

## I. INTRODUCTION

Polymeric systems exhibit diverse phenomena that span a wide range length and time scales.[1,2] Examples include biopolymers such as proteins,[3] and synthetic polymers in both melts and in solution.[1,2,4] In principle, one can conceive of modeling the diverse length and time scales that range over orders of magnitude using simulations based on detailed Hamiltonians to probe all motions in a statistically meaningful fashion.[5,6] However, such an approach is not just hopelessly expensive but is also unlikely to be informative if one is interested in a specific window of length and time scales.[4,7] For the latter it suffices to implement simulation methods and potential functions designed to probe a specific realm of interest.[4,7]

The most straightforward approach would be to carry out molecular dynamics simulations in a mean-field solvent and polymers modeled using holonomic constraints. The latter allows us to eliminate high frequency modes, which leads to the use of larger time steps and access to slower motions sampled on realistic time scales. This is a reasonable approach if the time scales for simulated motions are well separated from the time scales of motions that are ignored.[8–10] However, macromolecular binding reactions are known to involve small and intermediate-scale chain motions that are likely to be linked to solvation and desolvation processes.[11–13] In order to study such processes it is necessary to probe the coupling between local chain flexibility, averaged solvent degrees of freedom, and large-scale motions of associating proteins and their substrates. This is realizable using hybrid methods[5,7,14,15] where Monte Carlo simulations[16,17] with “nonphysical” moves[5] designed to probe the effect of intramolecular conformational flexibility are incorporated into Brownian dynamics simulations[8] of association-dissociation reactions of either small molecule ligands and proteins or pairs of macromolecules. The idea is to carry out Monte Carlo simulations on specific substruc-

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tures wherein the degrees of freedom are individual torsion angles or sets of torsion angles. Issues that arise in torsional space molecular dynamics and hybrid torsional space Monte Carlo simulations,[18–20] are best analyzed using model systems such as a serial chain of point masses.

A serial chain[21] of point masses connected by bonds of fixed length and fixed bond angles is a reasonable model for simulating the equilibrium properties of isolated polymer chains or independent substructures within larger macromolecules. The relevant degrees of freedom in such a system are the so-called soft internal degrees or torsion angles. This system has been of long standing interest in the polymer literature.[22,23] For a chain with $(n+1)$-point masses connected by $n$ bond lengths, $n-1$ bond angles, and $n-2$ torsion angles there are $3n-3$ internal degrees of freedom, and six remaining degrees of freedom for rigid body motion of the chain. When bond lengths and bond angles are frozen, there are only $n+4$ degrees of freedom corresponding to $n-2$ torsions and six degrees of freedom for rigid body motion.

For a Hamiltonian $H(\mathbf{p},\mathbf{q})$, written as a sum of kinetic $K(\mathbf{p})$ and potential $U(\mathbf{q})$ energy terms, where $\mathbf{q}$ denotes generalized coordinates and $\mathbf{p}$ the generalized momenta, the partition function in an $n$-$V$-$T$ ensemble, following integration over the all generalized momenta, is $Q=C\int \exp(-U(\mathbf{q})/k_BT)\det[G(\mathbf{q})]^{1/2}d\mathbf{q}$. Here, $\mathbf{G}(\mathbf{q})$ refers to a $(3n+3)\times(3n+3)$ mass-metric tensor the $(k,l)$th element of which is of the form $g_{kl}=\sum_{i=0}^{n+1}m_i(\partial\mathbf{r}_i/\partial q_k)\cdot(\partial\mathbf{r}_i/\partial q_l)\cdot\mathbf{r}_i$ denotes Cartesian coordinates of individual mass points $m_i$ in a space-fixed reference frame, $k_B$ is the Boltzmann constant, and $T$ is the temperature. Conversely, for a chain with fixed bond lengths and bond angles, the partition function, written in terms of the unconstrained "soft" generalized coordinates $\mathbf{q}_s$, i.e., the torsions alone, takes the form $Q=\int \exp[-U(\mathbf{q}_s)/k_BT]\sqrt{\det[\mathbf{G}_S(\mathbf{q}_s)]}d\mathbf{q}$, where $\mathbf{G}_s$ is a $(n+4)\times(n+4)$ reduced mass-metric tensor for the manifold defined by rigid bond lengths and bond angles. As is well known,[24–26] the reduced mass-metric tensor $\mathbf{G}_s$ is clearly not the same as the full mass-metric tensor $\mathbf{G}$. Furthermore, unlike $\det(\mathbf{G})$, which is typically independent of the values of $\mathbf{q}_s$, i.e., chain conformation, $\det(\mathbf{G}_s)$ is expected to depend nonlinearly on the values of the coordinates $\mathbf{q}_s$.[25–30]

### A. Implication of $\det(\mathbf{G}_s)$ for molecular simulations

Several researchers have studied the effect of constraints on the equilibrium statistics and rates of conformational transitions in molecular dynamics simulations for chains with frozen bond lengths and frozen bond angles.[28,31–38] Primarily because momenta conjugate to unconstrained degrees of freedom are set to zero,[39] constraining bond lengths and bond angles lead to artificial coupling between the unconstrained flexible degrees of freedom and introduces biases[22,24,39,25,28] that must be removed by adding a compensating potential $U_c$ of the form $U_c(\mathbf{q}_s)\propto -k_BT/2\ln[\det(\mathbf{G}_s)]$ (Refs. 25 and 27) to the original potential function $U(\mathbf{q}_s)$. Incorporation of compensating potentials into torsional space molecular dynamics is now standard practice[37,38,40] and important algorithmic improvements for the calculation of correction forces related to the compensating potential continue to be made[41] although some algorithms continue to ignore compensating potentials altogether.[42] However, for overdamped dynamics and state-to-state transition probabilities in torsional space Monte Carlo simulations, prescriptions regarding the use of compensating potentials related to $\det(\mathbf{G}_s)$ remain ambiguous.[43–46] Theodorou and co-workers[47] have shown that ratios of mass-metric tensor determinants must be included in the acceptance ratios for move sets that are based on concerted motions, i.e., for moves that vary collections of torsion angles between fixed ends of a chain. Hoffman and Knapp have adopted similar strategies in their "window move Monte Carlo" simulations.[48] If the goal is to design move sets for torsional space Monte Carlo simulations without loop closure, the question is as follows: Is it necessary to include terms related to the mass-metric tensor determinant $\det(\mathbf{G}_s)$? Unfortunately, the literature offers ambiguous advice for solving this important problem.[5,6,49] It is difficult to resolve these ambiguities without *a priori* knowledge regarding the conformational dependence of $\det(\mathbf{G}_s)$ and a direct comparison of thermodynamic averages between two types of simulations, viz., torsional space molecular dynamics simulations that include the Fixman potential and variants of torsional space Monte Carlo simulations.

In order to understand the nature of the biases imposed by constraints in molecular dynamics simulations without the Fixman potential and to decide on the correct course of action for Monte Carlo simulations it is essential that we understand the magnitude and the nature of the conformational dependence of $\det(\mathbf{G}_s)$ for a serial chain with frozen bond lengths and bond angles.[49] This is our objective in the current paper. We focus on answering two important questions, namely: (1) What is the nature of the conformational dependence of $\det(\mathbf{G}_s)$, i.e., what type of conformers maximize $\det(\mathbf{G}_s)$ and what type of conformers minimize $\det(\mathbf{G}_s)$? (2) What is the magnitude of variation in $\ln[\det(\mathbf{G}_s)]$ between conformers that maximize $\det(\mathbf{G}_s)$ and those that minimize $\det(\mathbf{G}_s)$?

In order to answer the questions raised above we need a method for computing $\det(\mathbf{G}_s)$. The algorithm should permit a comprehensive analysis of the structure of $\mathbf{G}_s$ and a physical interpretation tailor made to address the questions raised above. An important upshot of our current study is the refinement of an $O(n)$ algorithm proposed by Saha,[50,51] which is an algorithm for the inverted inertia matrix of serial robot arms, for computing $\det(\mathbf{G}_s)$. The refined algorithm will have practical use in future work on Monte Carlo simulations.

In order to provide a rationale for our adaptation of Saha's algorithm,[51] we briefly review methods drawn from both the polymer and robotics literatures for computing $\det(\mathbf{G}_s)$ and quantities related to $\mathbf{G}_s$. This is followed by a derivation of an exact recursion relation for $\det(\mathbf{G}_s)$ for a serial chain with constrained bond lengths and bond angles. In the results section we analyze the nature and magnitude of $\det(\mathbf{G}_s)$ for different chain conformers and varying numbers of torsional degrees of freedom. *Our work represents the first systematic analysis of the variation of* $\det(\mathbf{G}_s)$ *with chain conformational and chain length. The main finding is that* $\det(\mathbf{G}_s)$ *is* *maximized for spatial conformations and minimized for planar conformations*. We conclude with a brief discussion on the implication of our findings for the design of torsional space Monte Carlo simulations in polymeric systems.

### B. Algorithms for computing det($\mathbf{G}_s$)

*Calculation of* det($\mathbf{G}_s$)—*Fixman*'s *method*: The most popular approach in the polymer literature relies on the astute observations made by Fixman[25,27] regarding the relationship between the determinant of the full mass-metric tensor, det($\mathbf{G}$), which is easily calculated,[25] and the determinant of the reduced mass-metric tensor, det($\mathbf{G}_s$). Fixman showed that, $\det(\mathbf{G}_s)=\det(\mathbf{G})\det(\mathbf{H})$. The elements of $\mathbf{H}$, viz., $h_{kl}=\Sigma_{i=0}^{n+1}(1/m_i)(\partial q_k^H/\partial \mathbf{r}_i)\cdot(\partial q_l^H/\partial \mathbf{r}_i)$, where $q_l^H$ and $q_k^H$ refer to the constrained generalized coordinates or hard modes, are easier to compute, when compared to the elements of $\mathbf{G}_s$. For the case of fixed bond lengths and flexible bond angles $\mathbf{H}$ is a tridiagonal matrix and det($\mathbf{H}$) can be obtained using a simple recursion relation. For rigid bond lengths and bond angles, the matrix $\mathbf{H}$ has band limit five, and although det($\mathbf{H}$) cannot be obtained using the same recursion relation as in Fixman's paper,[25] appropriate strategies for matrix decomposition may still ensure an $O(n)$ algorithm. However, since calculation of det($\mathbf{H}$) relies on prior knowledge of individual elements of the $\mathbf{H}$ matrix, generalization of Fixman's approach to chains with arbitrary constraints or long chains with frozen bonds is unlikely to be an efficient process.[38]

*Calculation of* det($\mathbf{G}_s$)—*methods from the robotics literature*: In the field of robotics, mass-metric tensors and their inverse play an integral part of algorithms for forward and inverse dynamics.[52–54] Within the robotics literature, there are two categories of algorithms to compute the mass-metric tensor determinant and associated gradients.[51] In the first approach, elements of the mass-metric tensor are determined individually[55,56] and the required determinants are calculated using techniques such as Cholesky decompositions,[57] the complexity of which grows as $O(n^3)$.[55,56] In the second approach, algorithms based on recursion relations reduce the computational complexity to $O(n)$.

One of the best-known $O(n)$ algorithms is based on the so-called spatial operator factorization technique developed by a group of researchers at the Jet Propulsion Laboratory.[38,58–61] These algorithms rely on a fundamental analogy between the dynamics of multibody robots and the recursive equations of Kallman filtering.[62] Two distinct factorizations are realized, namely, one for the mass-metric tensor and the second for the inverse of the mass-metric tensor,[58,59] both of which are similar to covariance factorizations[62] which produce highly efficient $O(n)$ algorithms both for the calculation of mass-metric tensor determinants and for forward and inverse dynamics in serial robotic systems and polymeric systems.[38,58–61,63] As an illustration of the latter, Jain has implemented a recursive algorithm based on spatial operator algebra that does not require explicit computation of the mass-metric tensor.[38] This method, available as part of the NEIMO software package,[63] is especially well suited to tree-topology and serial macromolecules with hard constraints.[38,63]

Spatial operator algebra clearly leads to a class of efficient algorithms for molecular dynamics in internal coordinate space. However, the use of this approach does not serve our twofold purpose of first, carrying out a direct analysis of the behavior of det($\mathbf{G}_s$) as a function of chain length and second, obtaining a physical interpretation regarding the nature of the conformational dependence of this quantity. Alternatively, Saha has proposed an approach based on application of Gaussian elimination to elements of the mass-metric tensor.[50,51] Saha has shown that in addition to preserving the recursive schemes necessary for $O(n)$ algorithms, the method of mass-metric tensor decomposition also provides a clear physical/geometric interpretation, which allows us to understand the magnitude and nature of the bias imposed by the presence of the term det($\mathbf{G}_s$) in the equilibrium partition function for a chain with constraints. Hence, we adapt Saha's algorithm[51] to the problem of interest, viz., the calculation, and analysis of det($\mathbf{G}_s$) as a function of varying numbers of torsional angles for serial chains with constrained bond lengths and bond angles.

## II. DERIVATION OF THE RECURSION RELATIONSHIP TO CALCULATE det($\mathbf{G}_s$)

*The polymer model*: Fig. 1 shows the geometry of the model system with $n+1$ point masses (labeled 0, 1, 2,..., $n$) connected by $n-1$ bond angles (labeled 1, 2,..., $n-1$) and $n-2$ torsion angles (labeled 1, 2,..., $n-2$). For an isolated serial chain with rigid bond lengths and bond angles, the generalized coordinates $\mathbf{q}_s=(\mathbf{a},\alpha,\beta,\gamma,\phi_1,\ldots,\phi_{n-2})$ are a combination of torsion angles, $(\phi_1,\ldots,\phi_{n-2})$, and rigid-body motions ($\mathbf{a}$,$\alpha$,$\beta$,$\gamma$). Let $\mathbf{R}_{zxz}(\alpha,\beta,\gamma)$ be a rotation matrix, parameterized using Euler angles in the $ZXZ$ convention,[64,65] and $\mathbf{a}$ be the translational vector for displacement of the polymer chain from the inertial frame in three-dimensional Cartesian space (Fig. 1). The equilibrium bond lengths are labeled as $L_i$ for $i=1,...,n$; bond angles are $\theta_j$ for $j=1,...,n-1$, and the torsion angles are $\phi_k$ for $k=1,...,n-1$. Reference frames $F_i$ are attached to each point mass $i$; $i=0,...,n$ such that we get the following.

(1) The axis $\vec{z}_i$ is along bond $i$; $i=1,...,n$; $\vec{z}_0$ is along bond 1.

(2) The axis $\vec{y}_0$ is such that $m_0$, $m_1$, and $m_2$ are contained in the plane $\vec{y}_0 O \vec{z}_0$; then, $\vec{x}_0=\vec{y}_0\times\vec{z}_0$.

(3) $F_1$ is parallel with frame $F_0$; the transformation from $F_0$ to $F_1$ is represented by a translation along the axis $\vec{z}_0$ with $L_1$.

(4) The transformation from $F_1$ to $F_2$ is composed from a rotation with the angle $\theta_1$ around axis $\vec{x}_1$ followed by a translation along the rotated $\vec{z}_1$ with $L_2$.

(5) The transformation from $F_{i-1}$ to $F_i$ is composed from a rotation with magnitude $\phi_{i-1}$ around $\vec{z}_{i-1}$ followed by a rotation with $\theta_{i-1}$ around the new $\vec{x}_{i-1}$ followed then by a translation with $L_i$ along the new $\vec{z}_i$ (Fig. 1).

Let $\mathbf{x}_0=[0\ 0\ 0]$ denote the relative position of mass $m_0$ in the frame of reference attached to the base of the chain—$F_0$, and $\mathbf{r}_0=\mathbf{a}$ be its absolute position, (Fig. 1). Likewise,

$$\mathbf{x}_1=[0\quad 0\quad L_1]^T,\qquad \mathbf{r}_1=\mathbf{R}_{zxz}(\alpha,\beta,\gamma)\mathbf{x}_1+\mathbf{a}, \tag{1}$$

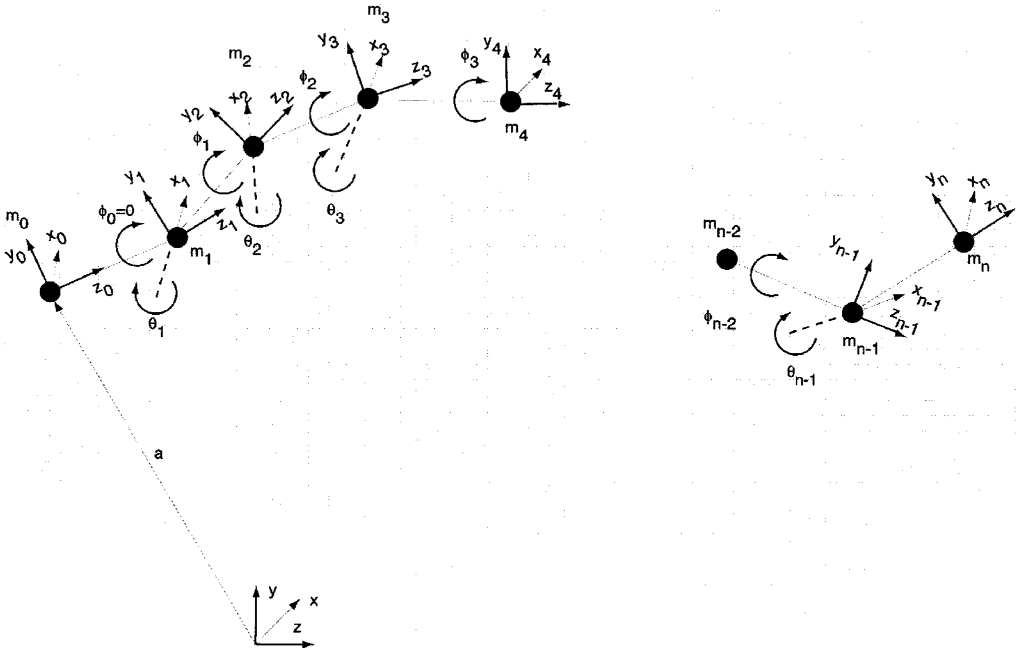

FIG. 1. Polymer model: Cartoon for the macroscopically serial chain with $n+1$ mass points, $n$-massless links, $n$-1 bond angles, and $n$-2 torsions. The base of the chain, mass-point $m_0$ is freely floating with respect to the inertial axes.

$$\mathbf{r}_2=\mathbf{r}_1+\mathbf{R}_{zxz}(\alpha,\beta,\gamma)\mathrm{rot}_x(\theta_1)[0 \quad 0 \quad L_2]^T \tag{2}$$

with

$$\mathrm{Rot}_z(\alpha)=\begin{bmatrix}\cos\alpha & -\sin\alpha & 0\\ \sin\alpha & \cos\alpha & 0\\ 0 & 0 & 1\end{bmatrix},$$

$$\mathrm{Rot}_x(\alpha)=\begin{bmatrix}1 & 0 & 0\\ 0 & \cos\alpha & -\sin\alpha\\ 0 & \sin\alpha & \cos\alpha\end{bmatrix}.$$

Note that due to the serial nature of the chain, the Cartesian coordinates for $i=3,...,n$,

$$\begin{aligned}\mathbf{r}_i=&\mathbf{r}_{i-1}+L_i\mathbf{R}_{zxz}(\alpha,\beta,\gamma)\\ &\times\mathbf{R}_{i-1}(\phi_1,\ldots,\phi_{i-2};\theta_1,\ldots,\theta_{i-2})\hat{\mathbf{u}}_i(\phi_{i-1},\theta_{i-1}),\end{aligned} \tag{3}$$

where $\mathbf{R}_{i-1}$ is a rotation matrix that describes the orientation of frame $i-1$ with respect to the base frame. This matrix can be computed by concatenating local changes in orientation as

$$\begin{aligned}&\mathbf{R}_{i-1}=\mathbf{R}_1^0(0,0)\mathbf{R}_2^1(0,\theta_1)\cdots\mathbf{R}_{i-1}^{i-2}(\phi_{i-2},\theta_{i-2}), \quad i=2,...,n\\ &\mathbf{R}_{k+1}^k(\phi_k,\theta_k)=\mathrm{Rot}_z(\phi_k)\mathrm{Rot}_x(\theta_k), \quad k=1,...,n-1.\end{aligned} \tag{4}$$

The vector $\hat{\mathbf{u}}_i$ is unitary, pointing in the direction of bond $i$ as seen in reference frame $i-1$ attached to the intersection of bonds $i-1$ and $i\cdot\hat{\mathbf{u}}_i=\mathbf{R}_i^{i-1}(\phi_{i-1},\theta_{i-1})\hat{\mathbf{e}}_3$; $\hat{\mathbf{e}}_3=[0\ 0\ 1]^T$.

We use the rigid-body transformation $[\mathbf{R}_{zxz}(\alpha,\beta,\gamma),\mathbf{a}]$ to describe the position and orientation of a frame of reference attached to the proximal end of the chain relative to the inertial frame. The position of any point on the polymer relative to the proximal end frame is a function of the torsions alone. Hence, the position of the $i$th point mass in the system with respect to inertial space will be

$$\mathbf{r}_i=\mathbf{R}_{zxz}(\alpha,\beta,\gamma)\mathbf{x}_i+\mathbf{a}. \tag{5}$$

*Kinetic energy in terms of the generalized velocities*: We first recast the mass matrix in a form that will allow us to compute the determinant using an $O(n)$ algorithm. The kinetic energy of the system is

$$K=\frac{1}{2}\sum_{i=0}^{n} m_i\dot{\mathbf{r}}_i^T\dot{\mathbf{r}}_i\,. \tag{6}$$

Position vectors of the point masses in the inertial frame take the form

$$\mathbf{r}_i=\mathbf{r}_{i-1}+L_i\tilde{\mathbf{R}}_i\hat{\mathbf{e}}_3, \quad i=3,...,n, \tag{7}$$

where $\tilde{\mathbf{R}}_i=\mathbf{R}_{zxz}(\alpha,\beta,\gamma)\mathbf{R}_i$ is the rotation matrix from the inertial frame to the frame $i$ in the chain and can be expressed as

$$\tilde{\mathbf{R}}_i=\tilde{\mathbf{R}}_{i-1}\mathbf{R}_i^{i-1}(\phi_{i-1},\theta_{i-1}), \quad i=2,...,n. \tag{8}$$

The velocity of the $i$th point mass is then:

$$\dot{\mathbf{r}}_i=\dot{\mathbf{r}}_{i-1}+L_i\dot{\tilde{\mathbf{R}}}_i\hat{\mathbf{e}}_3, \quad i=3,...,n. \tag{9}$$

The same quantity expressed in the $i$th reference frame becomes

$$\begin{aligned}&\tilde{\mathbf{R}}_i^T\dot{\mathbf{r}}_i=\tilde{\mathbf{R}}_i^T\dot{\mathbf{r}}_{i-1}+L_i\tilde{\mathbf{R}}_i^T\dot{\tilde{\mathbf{R}}}_i\hat{\mathbf{e}}_3,\\ &\mathbf{v}_i=\mathrm{Rot}_x(\theta_{i-1})^T\mathrm{Rot}_z(\phi_{i-1})^T\tilde{\mathbf{R}}_{i-1}^T\dot{\mathbf{r}}_{i-1}-\mathrm{Skew}(\hat{\mathbf{e}}_3L_i)\boldsymbol{\omega}_i,\end{aligned} \tag{10}$$

where $\boldsymbol{\omega}_i$ is the angular velocity of the frame $i$ relative to the inertial frame, but expressed in frame $i$ and Skew($\boldsymbol{\omega}$) is the skew symmetric matrix associate with $\boldsymbol{\omega}$:[66]

$$\boldsymbol{\omega}_i = \mathbf{R}_i^{i-1}(\phi_{i-1},\theta_{i-1})^T \boldsymbol{\omega}_{i-1} + \mathrm{Rot}_x(\phi_{i-1})^T \hat{\mathbf{e}}_3 \dot{\phi}_{i-1}, \quad i=3,\dots,n. \tag{11}$$

Substituting $\boldsymbol{\omega}_i$ from Eq. (11) into Eq. (10), $\mathbf{v}_i$ and $\boldsymbol{\omega}_i$ will be expressed as functions of $\mathbf{v}_{i-1}$ and $\boldsymbol{\omega}_{i-1}$ and $\dot{\phi}_{i-2}$. Therefore

$$\begin{aligned}\mathbf{v}_i =\ & \mathbf{R}_i^{i-1}(\phi_{i-1},\theta_{i-1})^T \mathbf{v}_{i-1} \\ & - L_i \mathrm{Skew}(\hat{e}_3) \mathbf{R}_i^{i-1}(\phi_{i-1},\theta_{i-1})^T \boldsymbol{\omega}_{i-1} \\ & - L_i \mathrm{Skew}(\hat{e}_3) \mathrm{Rot}_x(\theta_{i-1})^T \hat{\mathbf{e}}_3 \dot{\phi}_{i-1}, \quad i=3,\dots,n.\end{aligned} \tag{12}$$

In compact notation, Eqs. (10) and (11) can be written as

$$\begin{bmatrix} \boldsymbol{\omega}_i \\ \mathbf{v}_i \end{bmatrix} = \mathbf{B}_{i,i-1} \begin{bmatrix} \boldsymbol{\omega}_{i-1} \\ \mathbf{v}_{i-1} \end{bmatrix} + \mathbf{p}_i \dot{\phi}_{i-1}, \quad i=3,\dots,n, \tag{13}$$

where $\mathbf{B}_{i,i-1}$ and $\mathbf{p}_i$ are given by

$$\mathbf{B}_{i,i-1} = \begin{bmatrix} \mathrm{Rot}_x(\theta_{i-1})^T \mathrm{Rot}_z(\phi_{i-1})^T & \mathbf{0}_{3\times 3} \\ -\mathrm{Skew}(L_i \hat{\mathbf{e}}_3) \mathrm{Rot}_x(\theta_{i-1})^T \mathrm{Rot}_z(\phi_{i-1})^T & \mathrm{Rot}_x(\theta_{i-1})^T \mathrm{Rot}_z(\phi_{i-1})^T \end{bmatrix}, \tag{14}$$

$$\mathbf{p}_i = \begin{bmatrix} \mathrm{Rot}_x(\theta_{i-1})^T \hat{\mathbf{e}}_3 \\ -\mathrm{Skew}(L_i \hat{\mathbf{e}}_3) \mathrm{Rot}_x(\theta_{i-1})^T \hat{\mathbf{e}}_3 \end{bmatrix}.$$

For the first three mass points, we have

$$\mathbf{v}_0 = \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T \dot{\mathbf{a}}, \tag{15}$$

$$\mathbf{v}_1 = \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T \dot{\mathbf{a}} - L_1 \mathrm{Skew}(\hat{\mathbf{e}}_3) \mathbf{J}_R \begin{bmatrix} \dot{\alpha} \\ \dot{\beta} \\ \dot{\gamma} \end{bmatrix}, \tag{16}$$

$$\boldsymbol{\omega}_2 = \mathrm{Rot}_x(\theta_1)^T \boldsymbol{\omega}_1 = \mathrm{Rot}_x(\theta_1)^T \mathbf{J}_R \begin{bmatrix} \dot{\alpha} \\ \dot{\beta} \\ \dot{\gamma} \end{bmatrix}, \tag{17}$$

$$\mathbf{v}_2 = \left\{ \begin{aligned} & \mathrm{Rot}_x(\theta_1)^T \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T \dot{\mathbf{a}} - [L_1 \mathrm{Rot}_x(\theta_1)^T \mathrm{Skew}(\hat{\mathbf{e}}_3) \\ & + L_2 \mathrm{Skew}(\hat{\mathbf{e}}_3) \mathrm{Rot}_x(\theta_1)^T] \mathbf{J}_R \begin{bmatrix} \dot{\alpha} \\ \dot{\beta} \\ \dot{\gamma} \end{bmatrix} \end{aligned} \right\}, \tag{18}$$

where

$$\mathbf{J}_R = \begin{pmatrix} \sin\beta\sin\gamma & \sin\beta\sin\gamma & 0 \\ \sin\beta\cos\gamma & -\sin\gamma & 0 \\ \cos\beta & 0 & 1 \end{pmatrix}.$$

In compact notation

$$\begin{bmatrix} \mathbf{v}_0 \\ \mathbf{v}_1 \\ \boldsymbol{\omega}_2 \\ \mathbf{v}_2 \end{bmatrix} = \mathbf{P}_1 \begin{bmatrix} \dot{\mathbf{a}} \\ \dot{\alpha} \\ \dot{\beta} \\ \dot{\gamma} \end{bmatrix}, \tag{19}$$

where

$$\mathbf{P}_1 = \begin{bmatrix} \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T & \mathbf{0}_{3\times 3} \\ \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T & -L_1 \mathrm{Skew}(\hat{\mathbf{e}}_3) \mathbf{J}_R \\ \mathbf{0}_{3\times 3} & \mathrm{Rot}_x(\theta_1)^T \mathbf{J}_R \\ \mathrm{Rot}_x(\theta_1)^T \mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T & -[L_1 \mathrm{Rot}_x(\theta_1)^T \mathrm{Skew}(\hat{\mathbf{e}}_3) + L_2 \mathrm{Skew}(\hat{\mathbf{e}}_3) \mathrm{Rot}_x(\theta_1)^T] \mathbf{J}_R \end{bmatrix}. \tag{20}$$

The expression for the kinetic energy can be written in a more concise form using spatial vectors,[58]

$$K=\frac{1}{2}\sum_{i=0}^{n} m_i\dot{\mathbf{r}}_i^T\dot{\mathbf{r}}_i=\frac{1}{2}[\dot{\mathbf{r}}_0^T\ \ \dot{\mathbf{r}}_1^T\ \ \boldsymbol{\omega}_2^T\ \ \dot{\mathbf{r}}_2^T\ \ \boldsymbol{\omega}_3^T\ \ \dot{\mathbf{r}}_3^T\ \ \cdots]\mathbf{M}\begin{bmatrix}\dot{\mathbf{r}}_0\\ \dot{\mathbf{r}}_1\\ \boldsymbol{\omega}_2\\ \dot{\mathbf{r}}_2\\ \boldsymbol{\omega}_3\\ \dot{\mathbf{r}}_3\\ \vdots\end{bmatrix},$$

$$\mathbf{M}=\mathbf{M}_1\oplus\mathbf{M}_2\oplus\mathbf{M}_3\oplus\cdots\oplus\mathbf{M}_n \tag{21}$$

with $\mathbf{M}_1=\left[\begin{smallmatrix} m_0\mathbf{1}_{3\times 3} & \mathbf{0}_{3\times 3}\\ \mathbf{0}_{3\times 3} & m_1\mathbf{1}_{3\times 3}\end{smallmatrix}\right]\cdot\mathbf{M}$ is constructed using a matrix direct sum ($\oplus$)

$$\mathbf{M}_i=\begin{bmatrix}\mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3}\\ \mathbf{0}_{3\times 3} & m_i\mathbf{1}_{3\times 3}\end{bmatrix},\quad i=2,...,n,$$

which is simply a block matrix constructed from a set of square matrices $\mathbf{M}_i$, $i=1,...,n$.

Using Eqs. (13) and (19) the kinetic energy is rewritten as a function of velocities expressed in frames attached to individual mass points as

$$\begin{bmatrix}\dot{\mathbf{r}}_0\\ \dot{\mathbf{r}}_1\\ \boldsymbol{\omega}_2\\ \dot{\mathbf{r}}_2\\ \boldsymbol{\omega}_3\\ \dot{\mathbf{r}}_3\\ \cdots\end{bmatrix}=\begin{bmatrix}\mathbf{R}_0 & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \cdots\\ \mathbf{0}_{3\times 3} & \mathbf{R}_1 & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \cdots\\ \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{1}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \cdots\\ \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{R}_2 & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \cdots\\ \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{1}_{3\times 3} & \mathbf{0}_{3\times 3} & \cdots\\ \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3} & \mathbf{R}_3 & \cdots\\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots\end{bmatrix}\times\begin{bmatrix}\mathbf{v}_0\\ \mathbf{v}_1\\ \boldsymbol{\omega}_2\\ \mathbf{v}_2\\ \boldsymbol{\omega}_3\\ \mathbf{v}_3\\ \cdots\end{bmatrix}. \tag{22}$$

We rewrite the combined velocity vector in compact form using the so-called natural orthogonal component (NOC) matrix introduced originally by Angeles and Lee[67] to relate angular and translational velocities of rigid bodies to the velocities of joints for serial robotic manipulators.[68] Saha used a decoupled form of the NOC matrix for the velocity vector of serial robotic manipulators with fixed base.[47] *In adapting Saha's algorithm, we have generalized it to apply for a chain of point masses connected by inextensible massless bonds, with the base of the chain freely floating.* Here

$$\begin{bmatrix}\mathbf{v}_0\\ \mathbf{v}_1\\ \boldsymbol{\omega}_2\\ \mathbf{v}_2\\ \boldsymbol{\omega}_3\\ \mathbf{v}_3\\ \vdots\end{bmatrix}=\mathbf{N}_1\mathbf{N}_d\begin{bmatrix}\dot{\mathbf{a}}\\ \dot{\alpha}\\ \dot{\beta}\\ \dot{\gamma}\\ \dot{\phi}_1\\ \vdots\end{bmatrix}. \tag{23}$$

The matrices $\mathbf{N}_1$ and $\mathbf{N}_d$ are of the form

$$\mathbf{N}_1=\begin{bmatrix}\mathbf{1}_{6\times 6} & \mathbf{0}_{6\times 6} & \mathbf{0}_{6\times 6} & \cdots & \mathbf{0}_{6\times 6}\\ \mathbf{0}_{6\times 6} & \mathbf{1}_{6\times 6} & \mathbf{0}_{6\times 6} & \cdots & \mathbf{0}_{6\times 6}\\ \mathbf{0}_{6\times 6} & \mathbf{B}_{3,2} & \mathbf{1}_{6\times 6} & \ddots & \mathbf{0}_{6\times 6}\\ \vdots & \vdots & \vdots & \ddots & \vdots\\ \mathbf{0}_{6\times 6} & \mathbf{B}_{n,2} & \mathbf{B}_{n,3} & \cdots & \mathbf{1}_{6\times 6}\end{bmatrix}_{6n\times 6n}, \tag{24}$$

$$\mathbf{N}_d=\begin{bmatrix}\mathbf{P}_{1(12\times 6)} & \mathbf{0}_{12\times 1} & \mathbf{0}_{12\times 1} & \cdots & \mathbf{0}_{12\times 1}\\ \mathbf{0}_{6\times 6} & \mathbf{p}_{3(6\times 1)} & \mathbf{0}_{6\times 1} & \cdots & \mathbf{0}_{6\times 1}\\ \mathbf{0}_{6\times 6} & \mathbf{0}_{6\times 1} & \mathbf{p}_{4(6\times 1)} & \cdots & \mathbf{0}_{6\times 1}\\ \vdots & \vdots & \vdots & \ddots & \vdots\\ \mathbf{0}_{6\times 6} & \mathbf{0}_{6\times 1} & \mathbf{0}_{6\times 1} & \cdots & \mathbf{p}_{n(6\times 1)}\end{bmatrix}_{6n\times(n+4)}.$$

The kinetic energy now becomes

$$K=\frac{1}{2}[\dot{\mathbf{a}}^T\ \ \dot{\alpha}\ \ \dot{\beta}\ \ \dot{\gamma}\ \ \dot{\phi}_1\ \ \cdots]\mathbf{N}_d^T\mathbf{N}_1^T\mathbf{M}\mathbf{N}_1\mathbf{N}_d\begin{bmatrix}\dot{\mathbf{a}}\\ \dot{\alpha}\\ \dot{\beta}\\ \dot{\gamma}\\ \dot{\phi}_1\\ \vdots\end{bmatrix}. \tag{25}$$

From Eq. (25) the generalized mass metric tensor is

$$\mathbf{G}_s=\mathbf{N}_d^T\mathbf{N}_1^T\mathbf{M}\mathbf{N}_1\mathbf{N}_d. \tag{26}$$

The matrix $\mathbf{P}_1$ can be further decomposed as $\mathbf{P}_{1_{(12\times 4)}}=\hat{\mathbf{P}}_{1_{(12\times 4)}}\hat{\mathbf{A}}_{1_{(4\times 6)}}$ where

$$\hat{\mathbf{P}}_1=\begin{bmatrix}\mathbf{1}_{3\times 3} & \mathbf{0}_{3\times 3}\\ \mathbf{1}_{3\times 3} & -\mathrm{Skew}(\hat{\mathbf{e}}_3L_1)\\ \mathbf{0}_{3\times 3} & \mathrm{Rot}_x(\theta_1)^T\\ \mathrm{Rot}_x(\theta_1)^T & -[\mathrm{Rot}_x(\theta_1)^T\mathrm{Skew}(\hat{\mathbf{e}}_3L_1)+\mathrm{Skew}(\hat{\mathbf{e}}_3L_2)\mathrm{Rot}_x(\theta_1)^T]\end{bmatrix}, \tag{27}$$

$$\hat{\mathbf{A}}=\begin{bmatrix}\mathbf{R}_{zxz}(\alpha,\beta,\gamma)^T & \mathbf{0}_{3\times 3}\\ \mathbf{0}_{3\times 3} & \mathbf{J}_R\end{bmatrix}, \tag{28}$$

$$\mathbf{N}_d=\hat{\mathbf{N}}_d\begin{bmatrix}\hat{\mathbf{A}} & \mathbf{0}_{6\times 6}\\ \mathbf{0}_{6\times 6} & \mathbf{1}_{(n-2)\times(n-2)}\end{bmatrix},\quad \hat{\mathbf{N}}_d =\begin{bmatrix}\hat{\mathbf{P}}_{1(12\times 6)} & \mathbf{0}_{12\times 1} & \cdots & \mathbf{0}_{12\times 1}\\ \mathbf{0}_{6\times 6} & \mathbf{p}_{3(6\times 1)} & \cdots & \mathbf{0}_{6\times 1}\\ \vdots & \vdots & \ddots & \vdots\\ \mathbf{0}_{6\times 6} & \mathbf{0}_{6\times 1} & \cdots & \mathbf{p}_{n(6\times 1)}\end{bmatrix}. \tag{29}$$

Finally, the desired determinant $\det(\mathbf{G}_S)$ is written as

$$\det(\mathbf{G}_S)=\sin^2\beta\,\det(\hat{\mathbf{G}}_S), \tag{30}$$

where

$$\hat{\mathbf{G}}_S=\hat{\mathbf{N}}_d^T\mathbf{N}_1^T\mathbf{M}\mathbf{N}_1\hat{\mathbf{N}}_d\,.$$

Each $6\times 6$ block along the diagonal of the $6n\times 6n$ matrix $\mathbf{N}_1^T\mathbf{M}\mathbf{N}_1$ in Eq. (30) may be interpreted as the extended mass of a composite chain consisting of mass points $i,\ldots,n$ connected by massless inextensible bonds.

*Calculation of* $\det(\mathbf{G}_s)$ *using Saha's algorithm*: Eq. (30) reduces the problem of interest to a calculation of $\det(\hat{\mathbf{G}}_s)$. This is accomplished using an $O(n)$ algorithm developed by Saha.[47] For the symmetric, positive-definite matrix $\hat{\mathbf{G}}_s$ a *reverse* Gaussian elimination is recursively applied[47,66] until we get to the block defined by the matrix $\hat{\mathbf{P}}_1$. This leads to the decomposition $\hat{\mathbf{G}}_s=\hat{\mathbf{U}}\hat{\mathbf{D}}\hat{\mathbf{U}}^T$, where $\hat{\mathbf{D}}$ is a $(n+4)\times(n+4)$ diagonal matrix and $\hat{\mathbf{U}}$ is a unit upper triangular matrix such that $\det(\hat{\mathbf{U}})=1$ and $\det(\hat{\mathbf{G}}_s)=\det(\hat{\mathbf{D}})$. Here

$$\hat{\mathbf{D}}=\begin{bmatrix}\mathbf{Q}_1 & 0 & 0 & 0 & 0\\ \cdot & \hat{m}_3 & 0 & 0 & 0\\ \cdot & \cdot & \hat{m}_4 & 0 & 0\\ \cdot & \cdot & \cdot & & 0\\ \cdot & \cdot & \cdot & \cdot & \hat{m}_n\end{bmatrix}, \tag{31}$$

$$\det(\hat{\mathbf{G}}_S)=\det(\mathbf{Q}_1)\prod_{i=3}^{n}\hat{m}_i\,. \tag{32}$$

In the reverse Gaussian elimination[51] procedure the matrix $\hat{\mathbf{G}}_S$ is reduced to a lower triangular form via successive premultiplication of the original matrix by a series of so-called elementary upper triangular matrices (EUTMs). This is to be contrasted with the conventional Gaussian elimination[51,69] procedure, which reduces the original matrix to an upper triangular form via successive premultiplication of the original matrix, by a series of so-called elementary lower triangular matrices, (ELTMs). Reverse Gaussian elimination is applied to take advantage of the fact that for the serial chain, elements of the decoupled form of the NOC matrices[28] are written in terms of $\mathbf{B}_{i,i-1}$ and $\mathbf{p}_i$,[14] and the elements of both these matrices depend only on the orientations of local frames of reference. The concatenation of local frames leads to simplified recursion relations for the elements of the final upper triangular matrix and the $O(n)$ algorithm for the evaluation of the determinant of $\hat{\mathbf{G}}_\mathbf{S}$. The main ideas behind the reverse Gaussian elimination procedure proposed by Saha[47] are summarized in the Appendix.

*Physical/geometric interpretation of scalar quantities*: Following Saha,[47] we interpret each scalar $\hat{m}_k$, $(k=3,\ldots,n)$ as the rotational inertia of the distal end of the chain that emanates from mass-point $m_k$ as measured about the axis of rotation parallel to the $k$th bond. Each of the scalars is calculated using the formula

$$\hat{m}_k=(\mathbf{p}_k)^T_{1\times 6}(\hat{\boldsymbol{\Psi}}_k)_{6\times 1},\quad \text{pivot at the } k\text{th step}. \tag{33}$$

Premultiplication of the matrix $\hat{\mathbf{G}}_S$ by an EUTM leads to a new matrix and the introduction of a column with zeros above the diagonal. For the $k$th step if we denote the resultant matrix as $\hat{\mathbf{G}}_\mathbf{S}^{(k)}$, the pivot element at the $k$th step corresponds to the diagonal element of the column above which all elements are zero. For $k=3,\ldots,n\hat{\boldsymbol{\Psi}}_k$ in Eq. (33) is obtained using recursion relations of the form,

$$\begin{aligned}&\hat{\boldsymbol{\Psi}}_k=\hat{\mathbf{M}}_k\mathbf{p}_k\,,\\ &\hat{\mathbf{M}}_k=\mathbf{M}_k+\mathbf{B}^T_{k+1,k}(\hat{\mathbf{M}}_{k+1}-\hat{\boldsymbol{\Psi}}_{k+1}\boldsymbol{\Psi}_{k+1})\mathbf{B}_{k+1,k}\,,\\ &\boldsymbol{\Psi}_k=\frac{\hat{\boldsymbol{\Psi}}_k}{\hat{m}_k},\\ &\mathbf{M}_k=\begin{bmatrix}\mathbf{0}_{3\times 3} & \mathbf{0}_{3\times 3}\\ \mathbf{0}_{3\times 3} & m_k\mathbf{1}_{3\times 3}\end{bmatrix},\quad k=3,\ldots,n,\\ &\hat{\mathbf{M}}_n=\mathbf{M}_n\,.\end{aligned} \tag{34}$$

The $6\times 6$ matrix $\mathbf{Q}_1$ is defined as

$$\mathbf{Q}_1=\hat{\mathbf{P}}_1^T\{\mathbf{M}_1\oplus[\mathbf{M}_2+\mathbf{B}^T_{3,2}(\hat{\mathbf{M}}_3+\hat{\boldsymbol{\Psi}}_3\boldsymbol{\Psi}_3^T)\mathbf{B}_{3,2}]\}\hat{\mathbf{P}}_1\,. \tag{35}$$

The determinant of $\mathbf{Q}_1$ can be evaluated analytically or numerically and the desired determinant of the reduced mass-metric tensor is

$$\det(\mathbf{G}_s)=\sin^2\beta\,\det(\mathbf{Q}_1)\prod_{i=3}^{n}\hat{m}_i \tag{36}$$

## III. ANALYSIS OF det($\mathbf{G}_s$) AS A FUNCTION OF INCREASING NUMBERS OF TORSION ANGLES

We now proceed to analyze the nature and magnitude of the conformational dependence of $\det(\mathbf{G}_s)$ for serial chains of different lengths in different conformations. In the following discussion all references to $\det(\mathbf{G}_s)$ in actuality refer to $\det(\hat{\mathbf{G}}_s)$, which is directly related to $\det(\mathbf{G}_s)$ as shown in Eq. (30). We calculate $\det(\hat{\mathbf{G}}_s)$ using the recursion relations in Eqs. (32), (33), (34), and (35). We focus our attention on the nature of two types of conformations, viz., those that maximize $\det(\mathbf{G}_s)$, and those that minimize this quantity. In general, we find that spatial conformers have larger values for $\det(\mathbf{G}_s)$ when compared to planar conformers. In all of our calculations, all bond lengths were set to be 1 Å, masses were set to unity, and all bond angles were fixed at 109°. The fact that planar conformations minimize $\det(\mathbf{G}_s)$ is valid regardless of the value of bond angle. In what follows, $n$ denotes the number of mass points and $n_\phi$ denotes the number of torsions.

Analysis of the conformational variation of det($\mathbf{G}_s$) for $n=4$ and 5: We first evaluate the dependence of det($\mathbf{G}_s$) on the torsion angles by calculating this determinant for all possible conformations for chains with $n=4$ and $n=5$. Figure 2 shows the variation of det($\mathbf{G}_s$) as a function of $\phi$ for $n=4$. Our results are in agreement with results reported in the literature.[29,35] A contour plot of det($\mathbf{G}_s$) as a function of torsion angles $\phi_1$ and $\phi_2$ is shown in Fig. 3 for the chain with $n=5$. For $n=4$, det($\mathbf{G}_s$) is minimal for values of $\phi \approx 0°$ and $\phi \approx \pm 180°$ whereas det($\mathbf{G}_s$) is maximal for $\phi \approx \pm 90°$. Similarly for $n=5$, det($\mathbf{G}_s$) is minimized for $(\phi_1, \phi_2) \approx 0°$ and $(\phi_1, \phi_2) \approx \pm 180°$ whereas det($\mathbf{G}_s$) is maximal for $(\phi_1, \phi_2) \approx \pm 90°$. Setting $\phi_i \approx 0°$ or $\phi_i \approx 180°$ for $i=1$ or 2 and $\phi_j \approx \pm 90°$ for $j=1$ or 2 leads to local extrema, as shown in Fig. 3.

Extrema of det($\mathbf{G}_s$) for longer chains: Ideally, one would like to enumerate all possible conformations, compute det($\mathbf{G}_s$) for each conformer, and analyze the resultant hypersurface. However, exhaustive enumeration is not feasible because of rapid growth in the number of conceivable conformers. Therefore, we simplify the analysis by restricting our attention to conformers generated by combinations of two torsion angle values, viz., $\phi_i \approx \pm 90°$ and $\phi_i \approx 180°$ or 0°. For chains of length $n$ with $n_\phi$ torsion angles, we generated $2^{n_\phi}$ conformations. The procedure we use is as follows: for a chain with $n_\phi + 1$ torsion angles, we start with each of the $2^{n_\phi}$ conformers that minimize or maximize det($\mathbf{G}_s$) for a chain with $n_\phi$ torsion angles, and use a Hooke-Jeeves optimization[69] scheme to calculate the determinant for extremal conformations chains extended by one bond. This procedure yields conformers that can be clustered into two distinct sets, viz., the set of conformers, referred to as {Max}, which corresponds to combinations of torsion angles that maximize det($\mathbf{G}_s$) and a second set of conformers, referred to as {Min}, which is generated by combinations of $\phi$ angles that minimize det($\mathbf{G}_s$). For a chain with $n_\phi$ angles, there are $2^{n_\phi}$ local minima in the set {Min} and $2^{n_\phi}$ local maxima in the set {Max}.

Nature of conformers that minimize/maximize det($\mathbf{G}_s$): The two sets {Min} and {Max} comprise conformations that are both regular and random-coil-like. The ratio of the number of random coil[70] to the number of regular conformations is roughly similar in both sets since the values of the torsion angle, which minimize the metric tensor determinant, are $\approx \pm 180°$, whereas those that maximize it are $\approx \pm 90°$. Figures 4–7 show the extreme conformations within each set {Min} and {Max} for a chain with $n_\phi = 8$. Note that the conformations shown in Figs. 4 and 7 are not all self-avoiding. Although planar sheets/strands are not conformers that globally minimize the value of det($\mathbf{G}_s$), they are the only representative conformations from the set {Min} that are both well ordered and free of steric clashes. Similar arguments hold for spatial helices that maximize the value of det($\mathbf{G}_s$).

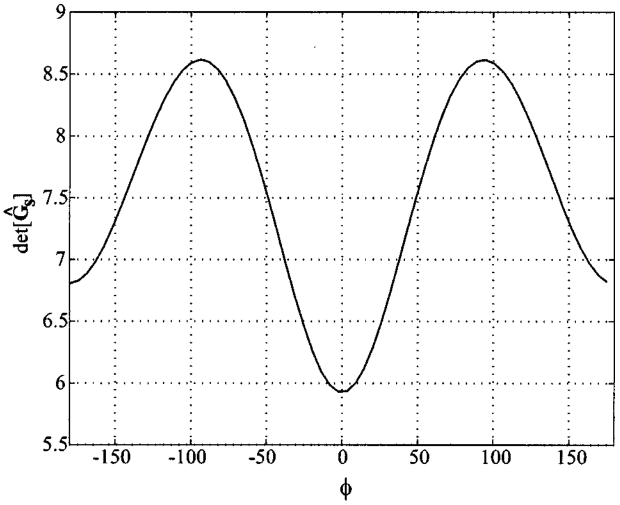

FIG. 2. Plot of det($\hat{\mathbf{G}}_s$) vs $\phi$ for a chain with four mass points, $n_\phi = 1$.

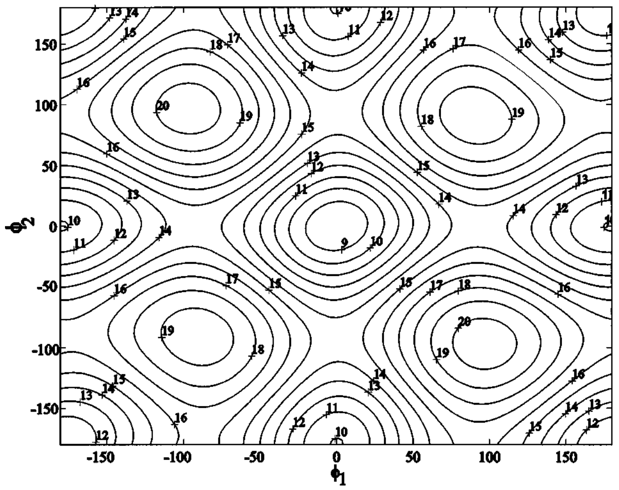

FIG. 3. Contour plot of det($\hat{\mathbf{G}}_s$) for a chain with five mass-points, $n_\phi = 2$. The two axes show the two torsion angles $\phi_1$ and $\phi_2$.

Behavior of det($\mathbf{G}_s$) as a function of $n_\phi$: Analyzing the range of det($\mathbf{G}_s$) values within and between the sets {Min} and {Max} provides a sense of how det($\mathbf{G}_s$) varies across contiguous regions in multidimensional space. We have quantified the influence of the number of torsions $n_\phi$ on the value of det($\mathbf{G}_s$) for the type of extrema shown in Figs. 4–7. In the analysis that follows, for a chain of length $n_\phi$, we use the notations described below.

(1) $G_1$: Is the value of det($\mathbf{G}_s$) for the conformer that corresponds to the global minimum.

(2) $G_2$: Is the maximum value of det($\mathbf{G}_s$) in the set {Min}.

(3) $G_3$: Is the smallest possible value of det($\mathbf{G}_s$) for conformers in the set {Max}.

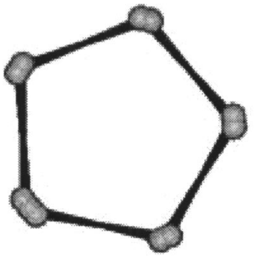

FIG. 4. Self-intersecting *planar* conformation ∈ {Min} with $n_\phi = 8$ for which the determinant det($\hat{\mathbf{G}}_s$) is a global minimum.

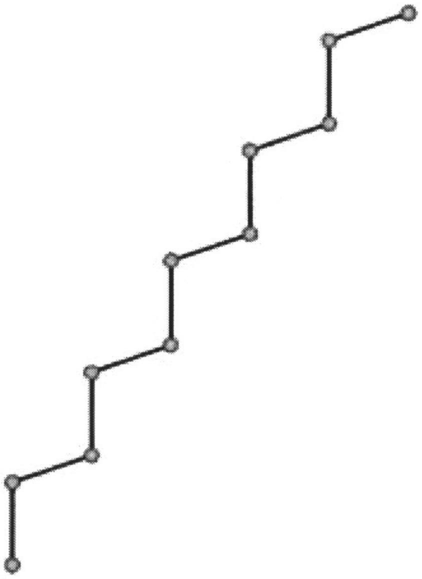

FIG. 5. Regular, sterically realizable planar conformation $\in\{\text{Min}\}$ with $n_\phi = 8$ for which the determinant $\det(\hat{\mathbf{G}}_s)$ is a local minimum.

(4) $G_4$: Is the value of $\det(\mathbf{G}_s)$ for the global maximum.

Variation of $\det(\mathbf{G}_s)$ for transitions between conformers within {Min} or {Max}: In Fig. 8 we show a plot of the ratio $G_2/G_1$ as a function of chain length. This quantity assesses the degree of variation in $\det(\mathbf{G}_s)$ values for conformers within the set {Min}. Variations between the extrema within the set {Min} are small. More importantly, in molecular simulations we would be interested in quantities related to $\ln[\det(\mathbf{G}_s)]$, and from Fig. 8 it is clear that for regions of conformation space corresponding to those in the set {Min} the degree of variation in $\ln[\det(\mathbf{G}_s)]$ is negligible. Similar conclusions result from an analysis of the ratio of $G_4/G_3$ as a function of chain length for conformers that belong to the set {Max}.

Variation of $\det(\mathbf{G}_s)$ for transitions between conformers that are in different sets, viz., {Min} and {Max}: We now proceed to analyze the behavior of $\det(\mathbf{G}_s)$ for conformers drawn from the two different sets, namely, {Min} and {Max}. In Fig. 9, we show a plot of the ratio $\log_{10}(G_3/G_2)$ as a function of $n_\phi$. Clearly, the minimal value of $\det(\mathbf{G}_s)$ over all conformations that belong to the set {Max}, $G_3$ remains well separated from the maximum value of $\det(\mathbf{G}_s)$ over all conformations that belong to the set {Min}, $G_2$. This suggests that the change in $\det(\mathbf{G}_s)$ is quite drastic for transitions between spatial and planar conformers.

FIG. 6. Regular, sterically realizable *spatial* conformation $\in\{\text{Max}\}$ with $n_\phi = 8$ for which the determinant $\det(\hat{\mathbf{G}}_s)$ is a local maximum.

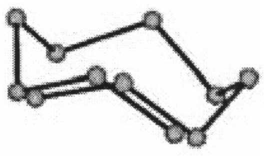

FIG. 7. Self-intersecting spatial conformer $\in\{\text{Max}\}$ with $n_\phi = 8$ for which the determinant $\det(\hat{\mathbf{G}}_s)$ is a global maximum.

Decomposing the contributions to $\det(\mathbf{G}_s)$: From Eq. (32), it follows that the determinant $\det(\hat{\mathbf{G}}_s)$ is a product of two components.

(1) In the first term $\Pi_{i=3}^{n}\hat{m}_i$ each $\hat{m}_i$ denotes the rotational inertia of the distal end of the chain that emanates from mass-point $m_i$ as measured about the axis of rotation parallel to the $i$th bond. The product is the mass-metric tensor determinant for a chain with its proximal end fixed in space.

(2) The second term $\det(\mathbf{Q}_1)$ represents the effect of the floating base on the mass-metric tensor determinant. The term $\det(\mathbf{Q}_1)$ reflects the coupling between the rigid body coordinates (spatial degrees of freedom) and chain conformation (internal coordinates). This coupling enters the expression for $\mathbf{Q}_1$ through the terms $\hat{\mathbf{\Psi}}_3$ and $\hat{\mathbf{M}}_3$. $\det(\mathbf{Q}_1)$, is a measure of the conformation-dependent translational and orientational entropy of the chain.

In order to estimate the relative contribution of the two components, $\Pi_{i=3}^{n}\hat{m}_i$ and $\det(\mathbf{Q}_1)$ to the value of $\det(\mathbf{G}_s)$ we compute the ratio $F = \sqrt{\det(\mathbf{Q}_1)/\Pi_{i=3}^{n}\hat{m}_i}$ as a function of $n_\phi$ for conformations that constitute the upper and lower bounds in the two sets {Min} and {Max}. Results so obtained are shown in Fig. 10. The ratio $F$ exhibits different behavior for extrema drawn from the two sets {Min} and {Max}, respectively. Whereas $F$ decreases as $n_\phi$ increases for conformers from the set {Min} it increases for conformers from the set {Min}. Upon comparison of the results from Figs. 8 and 9 to those in Fig. 10, we find that the evolution of the ratio

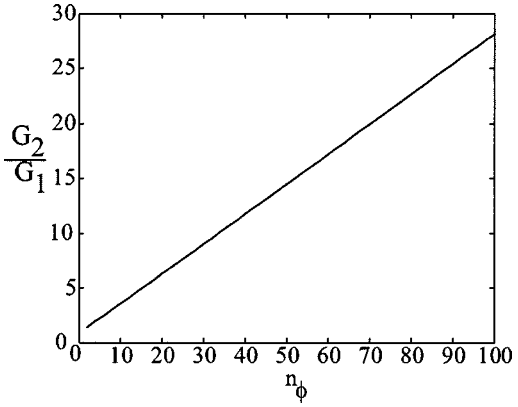

FIG. 8. Variation of the ratio $G_2/G_1$ as a function of $n_\phi$. $G_2$ and $G_1$ are defined in the text. This ratio indicates that the extent of variation of $\det(\mathbf{G}_s)$ and especially of $\ln[\det(\mathbf{G}_s)]$ with $n_\phi$ is negligible for conformers drawn from the set {Min}. Similar results are obtained for the ratio $G_4/G_3$ as a function of $n_\phi$.

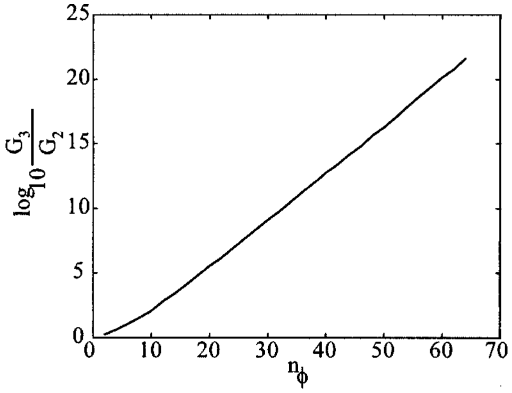

FIG. 9. Variation of the ratio $G_1/G_2$ as a function of $n_\phi$. This ratio quantifies the variation in det($\mathbf{G}_s$) for transitions between spatial and planar conformers. In this case, the variation of the ratio of det($\mathbf{G}_s$) or the ratio of ln[det($\mathbf{G}_s$)] is not negligible.

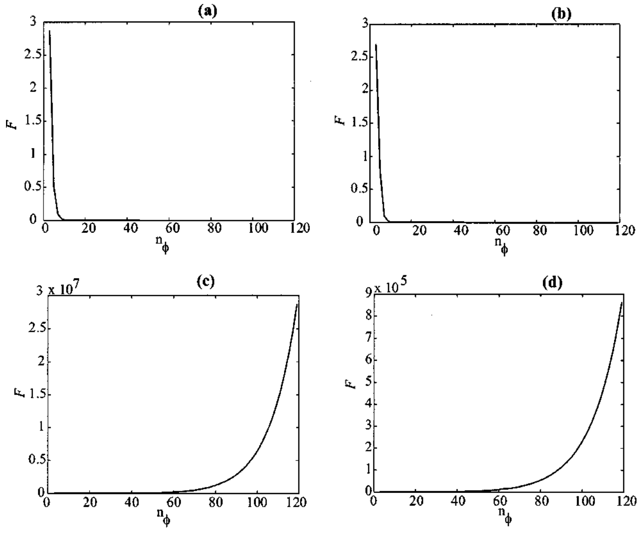

FIG. 10. Plots of $F=\sqrt{\det(\mathbf{Q}_1)/\Pi_{i=3}^{n} m_i'}$, the ratio of spatial versus conformational contributions to det($\mathbf{G}_s$), as a function of $n_\phi$. (a) For the upper bound in the set {Max}; (b) for the lower bound in the set {Max}; (c) for the upper bound in the set {Min}; and (d) for the lower bound in the set {Min}.

$G_2/G_1$ (and $G_4/G_3$) as a function of $n_\phi$ is mainly influenced by the behavior of det($\mathbf{Q}_1$). Conversely, the product $\Pi_{i=3}^{n}\hat{m}_i$ is the main factor in the evolution of the ratio $\log_{10}(G_4/G_3)$. Furthermore, det($\mathbf{Q}_1$) decreases with increasing $n_\phi$ whereas, $\Pi_{i=3}^{n}\hat{m}_i$ continues to increase as a function of chain length. This result is illustrated by Fig. 11, which plots the variation of

$$\ln(q_1/q_2)=\ln\sqrt{\det(\mathbf{Q}_1)\text{ for lower bound in}\{\text{Max}\}/\det(\mathbf{Q}_1)\text{ for upper bound in}\{\text{Min}\}}$$

and $\ln(m_1/m_2)=\ln(\Pi_{i=3}^{n}\hat{m}_i$ for lower bound in{Max}/$\Pi_{i=3}^{n}\hat{m}_i$ for upper bound in{Min}) as a function of $n_\phi$. Our results support the following conclusion: the variation in the behavior of det($\mathbf{G}_s$) for conformational transitions between the sets {Min} and {Max} does not lie in inertial quantities associated with det($\mathbf{Q}_1$) or ln[det($\mathbf{Q}_1$)], which quantifies the translational and orientational entropy of the chain. Instead, the differences are mainly due to contributions from inertial quantities associated with internal coordinates, i.e., by terms related to the conformational entropy of the chain.

## IV. SUMMARY

We have carried out a systematic analysis of the nature and magnitude of the conformational dependence of det($\mathbf{G}_s$). This topic has been an issue of intense scrutiny and debate in the polymer literature[28–30,32–34,26,35,36,23] and has spurred the development of elegant proposals for computing det($\mathbf{G}_s$) and associated quantities.[9,25,27,38,51] However, a systematic analysis of the conformational dependence of det($\mathbf{G}_s$) is missing. To some extent, this reflects the continued belief that computing det($\mathbf{G}_s$) is challenging,[38,49] a belief that is endorsed by the lack of this analysis in any of the original algorithmic papers.[25,38]

In order to carry out the proposed analysis we have adapted and refined a novel algorithm developed in the robotics literature.[50,51] A complete derivation of this $O(n)$ algorithm has been provided in Sec. II. In Sec. III, we carried out a systematic analysis of the conformational dependence of det($\mathbf{G}_s$). Our conclusions are as follows: (1) det($\mathbf{G}_s$) is maximized for spatial conformers and minimized for planar conformations. (2) The difference in det($\mathbf{G}_s$) between spatial and planar conformers is significant and, as one would logically expect,[27] this difference increases with increasing chain length. (3) The proposed algorithm for calculating det($\mathbf{G}_s$) is unique and novel in that it allows us to decompose the distinct contributions made by spatial variables or translational plus orientational entropy [det($\mathbf{Q}_1$)] and internal coordinates ($\Pi_{i=3}^{n}\hat{m}_i$) or conformational entropy to det($\mathbf{G}_s$). The extent of coupling between the two quantities is such that the dominant contributions to the variation of det($\mathbf{G}_s$) with conformation do not come from the coupling between conformational and translational plus orientational quantities. Instead, the main source of conformational heterogeneity of det($\mathbf{G}_s$) arises from quantities that depend on the torsion angles alone. We have been able to arrive at all of these conclusions because of the algorithm used to compute det($\mathbf{G}_s$), a full derivation of which has been provided in Sec. II.

*Implications for torsional space Monte Carlo simulations:* As noted in Sec. I A, ambiguous suggestions have been made regarding the role of det($\mathbf{G}_s$) in torsional space Monte Carlo simulations. Consider the following situation: suppose

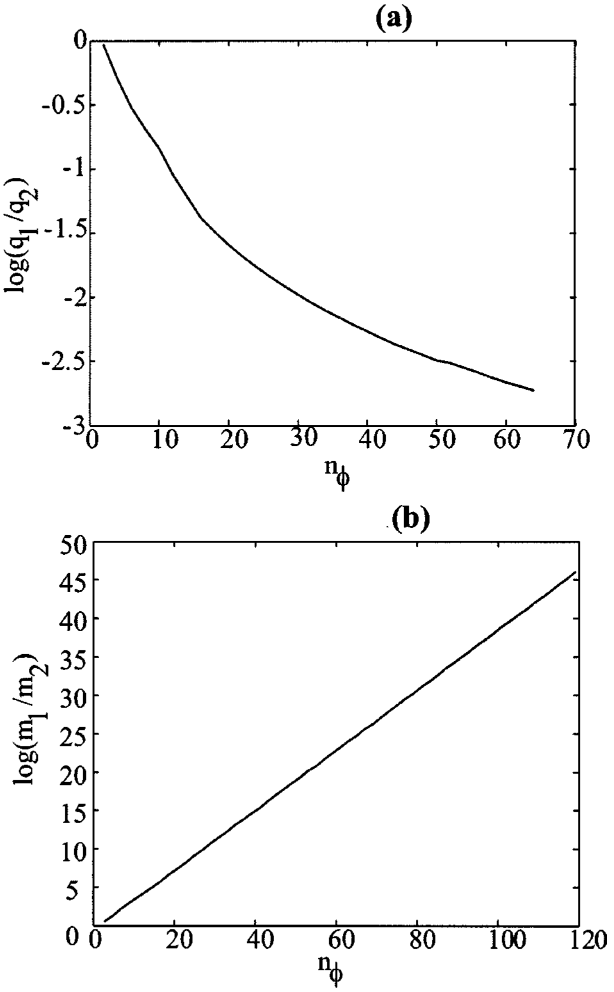

FIG. 11. Variation of

$$\ln(q_1/q_2)=\ln\frac{\sqrt{\det(\mathbf{Q}_1)\text{ for lower bound in }\{\text{Max}\}}}{\det(\mathbf{Q}_1)\text{ for upper bound in }\{\text{Min}\}}$$

as a function of $n_\phi$; (b) variation of $\ln(m_1/m_2)$ as a function of $n_\phi$.

a proposed move to change torsion angles takes the chain from conformation i to j. In order to ensure detailed balance we require that: $\rho_{eq}(\mathrm{i})\alpha(\mathrm{i}\rightarrow\mathrm{j})\mathrm{acc}(\mathrm{i}\rightarrow\mathrm{j})=\rho_{eq}(\mathrm{j})\alpha(\mathrm{j}\rightarrow\mathrm{i})\mathrm{acc}(\mathrm{j}\rightarrow\mathrm{i})$ where $\rho_{eq}(\mathrm{i})$ and $\rho_{eq}(\mathrm{j})$ are the equilibrium weights associated with conformations i and j, respectively; $\alpha(\mathrm{i}\rightarrow\mathrm{j})$ is the probability of making a transition between conformers i and j, which we shall mandate is symmetric, i.e., $\alpha(\mathrm{i}\rightarrow\mathrm{j})=\alpha(\mathrm{j}\rightarrow\mathrm{i})$. Finally, $\mathrm{acc}(\mathrm{i}\rightarrow\mathrm{j})$ denotes the probability of accepting a trial move from i to j. The likelihood of accepting a conformational transition i→j is dictated by the ratio: $A=\mathrm{acc}(\mathrm{i}\rightarrow\mathrm{j})/\mathrm{acc}(\mathrm{j}\rightarrow\mathrm{i})$. The standard literature on molecular simulations provides three drastically different suggestions for the form of $A$. These are as follows: (a) $A=\det[\mathbf{G}_s(\mathrm{j})]^{1/2}\exp(-\beta U_{\mathrm{j}})/\det[\mathbf{G}_s(\mathrm{i})]^{1/2}\exp(-\beta U_{\mathrm{i}})$, (b) $A=\det[\mathbf{G}_s(\mathrm{i})]^{1/2}\exp(-\beta U_{\mathrm{j}})/\det[\mathbf{G}_s(\mathrm{j})]^{1/2}\exp(-\beta U_{\mathrm{i}})$, or (c) $A=\exp\{-\beta[U_{\mathrm{j}}-U_{\mathrm{i}}]\}$. The acceptance ratios may be written in concise form as $A=\mathrm{acc}_G(\mathrm{i}\rightarrow\mathrm{j})\mathrm{acc}_B(\mathrm{i}\rightarrow\mathrm{j})/\mathrm{acc}_G(\mathrm{j}\rightarrow\mathrm{i})\mathrm{acc}_B(\mathrm{j}\rightarrow\mathrm{i})=A_GA_B$, where $A_G$ denotes the contribution from $\det(\mathbf{G}_s)$ or $\ln[\det(\mathbf{G}_s)]$ and $A_B$ denotes the contribution from relative Boltzmann weights. At issue, is the correct form for $A_G$. Frenkel and Smit[5] suggest the use of option (a) which corresponds to using the form of the integrand of the torsional space partition realized upon integration over all nonzero momenta (see Sec. I A). Allen and Tildesley[6] recommend the use of option (b) which corresponds to the incorporation of a Fixman potential to remove an ostensible bias. Finally, almost all torsional space Monte Carlo simulations choose option (c), i.e., the terms involving $\det(\mathbf{G}_s)$ are ignored, i.e., $A_G=1$.[44,49]

What is the correct form for $A_G$? In torsional space molecular dynamics simulations, conformations are sampled from a probability density of the form: $\rho(\mathbf{q}_s)\propto\sqrt{\det[\mathbf{G}_s(\mathbf{q}_s)]}\exp[-\beta U(\mathbf{q}_s)]$. As is well known, analysis of equilibrium statistics and rates of conformational transitions obtained from molecular dynamics simulations with some holonomic constraints indicates the presence of biases proportional to $\sqrt{\det(\mathbf{G}_s)}$, especially when compared to simulations based on the use of stiff restraints. These biases can be eliminated by incorporating a Fixman style compensation potential as discussed in Sec. I A. This is necessary in order to maintain congruence with statistics for systems where the constraints are replaced by stiff restraints. If the goal is to obtain similar congruence between torsional space Monte Carlo simulations and molecular dynamics simulations with stiff restraints, what is the correct choice for the form of $A_G$?

Based on our analysis, we conclude the following: if the proposed transition is from one conformation in set {Min} to another in the set {Min} or equivalently from one conformation in the set {Max} to another in the set {Max}, then for a prescribed chain length, as shown in Fig. 8, the changes in $\det(\mathbf{G}_s)$ are negligible. Consequently, all three options (a)–(c) outlined above will yield equivalent statistics. However, such small-scale conformational transitions are never guaranteed in torsional space where one sees large-scale lever arm effects for small changes in torsion angles,[47] i.e., most changes of torsion angles are likely to lead to transitions between planar and spatial conformers or vice versa.

Based on $\det(\mathbf{G}_s)$ values obtained using the algorithm presented in this work, we have tried to resolve the issue of choosing between the three different suggestions for the functional form of acceptance ratios. We accomplished this by comparing the statistics from torsional space Monte Carlo simulations to those obtained using molecular dynamics simulations with stiff bond lengths and bond angles. We will present the details of our calculations elsewhere. Here we present the main conclusions from our analysis. We conclude that the correct form for the acceptance ratio is option (c), i.e., $A_G=1$. One need worry about the biases due to mass-metric tensor determinants only in torsional space molecular dynamics simulations where the momenta conjugate to the soft modes are explicitly computed and specific momenta conjugate to the frozen bond lengths and bond angles are explicitly set to zero. The Fixman potential in molecular dynamics simulations eliminates biases by accounting for the loss in entropy associated with the freezing momenta conjugate to constrained coordinates. Upon elimination of the bias, we restore the Hamiltonian to one wherein the thermal and excess parts are separable. This is the starting point for the design of Monte Carlo simulations. In this limit, there is no *a priori* justification for the assumption of preexisting biases as is done in option (b) or for imposing biases related to volume elements as is done in option (a). This is especially true if one is interested in generating equilibrium statistics that are concordant with those obtained from simulations of systems wherein the constraints are replaced by stiff restraints. Hence, we propose that option (c) is the correct option for the acceptance ratio in Monte Carlo simulations without loop closure moves.[71–73] Our conclusions are in line with the results of Perchak *et al.*[74] who found that mass-metric tensor biases diminish as a function of increased friction in Brownian dynamics simulations and in the overdamped limit, where the momentum autocorrelation function decreases rapidly, the biases introduced due to artifacts of mass-metric tensor determinants are negligible.

## APPENDIX: DETAILS OF SAHA'S ALGORITHM

The decomposition of $\hat{\mathbf{G}}_s$ in Eq. (30) to $\hat{\mathbf{G}}_s = \hat{\mathbf{U}}\hat{\mathbf{D}}\hat{\mathbf{U}}$, where $\hat{\mathbf{D}}$ takes the form shown in Eq. (31) is accomplished using a reverse Gaussian elimination scheme proposed by Saha.[51] A common numerical approach in the computation of determinants is the reduction of the original matrix to a triangular form using Gaussian elimination. Details of the latter are available in standard linear algebra textbooks.[57] The main idea is that the original matrix is premultiplied by a sequence of so-called elementary lower triangular matrices (ELTM), where each ELTM is chosen such that premultiplication yields a new matrix with a column with zeros below the diagonal. Unlike conventional Gaussian elimination[57] which starts from the first column to make all elements except the top one zero, Saha's algorithm begins with the last column such that all elements excepting the bottom most one becomes zero. Hence, the name reverse Gaussian elimination. This procedure reflects the method of parameterization wherein the position coordinates of each mass point in the inertial frame are written in terms of the position coordinates of the preceding mass-points. Saha's method is applied to the symmetric, positivedefinite matrix $\hat{\mathbf{G}}_s$ shown in Eq. (30). The serial nature of the chain allows the procedure to be accomplished in $O(n)$ steps. The algorithm, paraphrased from Saha's work, are as follows.

(1) An EUTM is first defined. This is analogous to the elementary lower triangular matrix in conventional Gaussian elimination. This

$$\mathbf{E}_i = \mathbf{1}_{n' \times n'} - \boldsymbol{\alpha}_i \boldsymbol{\lambda}_i^T$$

matrix of order $n' = n+4$ and index $i$, is defined as $\boldsymbol{\alpha}_i = (\alpha_{li}, \dots, \alpha_{i-li}, 0, \dots, 0)^T$ and leads

$$\boldsymbol{\lambda}_i = (0, \dots, 0, 1, \dots, 0)^T$$

to the elimination of all elements above the pivot.

(2) For $i = n'$,

$$\mathbf{E}_{n'} = \begin{pmatrix} 1 & \cdots & -\alpha_{1n} \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 1 \end{pmatrix}_{n' \times n'} .$$

Premultiplying $\hat{\mathbf{G}}_\mathbf{s}$ defined in Eq. (30) by $\mathbf{E}_i$ for $i = n', \dots, 1$ yields an $n' \times n'$ lower triangular matrix $\hat{\mathbf{L}}$, i.e., $\mathbf{E}_l \cdots \mathbf{E}_{n'} \hat{\mathbf{G}}_s = \hat{\mathbf{L}}$. The latter is a consequence of the particular form for $\hat{\mathbf{G}}_s$ shown in Eq. (30). Alternatively, $\hat{\mathbf{G}}_s = \mathbf{E}_{n'}^{-1} \cdots \mathbf{E}_l^{-1} \hat{\mathbf{L}} = \hat{\mathbf{U}}\hat{\mathbf{L}}$ where $\mathbf{E}_{n'}^{-1} \cdots \mathbf{E}_l^{-1} \hat{\mathbf{L}} \equiv \hat{\mathbf{U}} = \mathbf{1}_{n' \times n'} + \overline{\boldsymbol{\alpha}}_{n'} \boldsymbol{\lambda}_{n'}^T, + \cdots + \boldsymbol{\alpha}_1 \boldsymbol{\lambda}_l^T$. The diagonal elements of $\hat{\mathbf{U}}$ are unity and consequently the symmetric, positive-definite lower triangular matrix $\hat{\mathbf{L}}$ may be rewritten as $\hat{\mathbf{L}} = \hat{\mathbf{D}}\hat{\mathbf{U}}^T$, where $\hat{\mathbf{D}}$ is an $n' \times n'$ diagonal matrix whose elements are the diagonal elements of $\hat{\mathbf{L}}$. The matrix $\hat{\mathbf{G}}_s$ is now decomposed as $\hat{\mathbf{G}}_s = \hat{\mathbf{U}}\hat{\mathbf{D}}\hat{\mathbf{U}}^T$. Since the determinant of a unit upper triangular matrix is unity, the required determinant $\det(\hat{\mathbf{G}}_s)$ is reduced to the determinant of the diagonal matrix $\det(\hat{\mathbf{D}})$.

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$$\mathbf{A}=\begin{pmatrix} \cos\gamma\cos\alpha-\cos\beta\sin\alpha\sin\gamma & \cos\gamma\cos\alpha+\cos\beta\sin\alpha\sin\gamma & \sin\gamma\sin\alpha \\ -\sin\gamma\cos\alpha-\cos\beta\sin\alpha\sin\gamma & -\sin\gamma\cos\alpha+\cos\beta\sin\alpha\sin\gamma & \cos\gamma\sin\alpha \\ \sin\beta\sin\gamma & -\sin\beta\cos\alpha & \cos\beta \end{pmatrix} \quad (\text{Ref. } 64).$$

Goldstein (Ref. 64) refers to the $ZXZ$ convention as the $x$ convention.

[66] A skew symmetric matrix associated with the vector $\mathbf{a}=(a_1,a_2,a_3)$ is

$$\tilde{\mathbf{a}}=\begin{pmatrix} 0 & -a_3 & a_2 \\ a_3 & 0 & -a_1 \\ -a_2 & a_1 & 0 \end{pmatrix}.$$

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