Monte Carlo simulations with a generalized detailed balance using the quantum-classical isomorphism

Yefim I. Leifman
Department of Mathematics and Statistics,
Bar-Ilan University,
52900, Ramat-Gan, Israel
leifmany@lycos.com
March 30, 2022

Abstract

The main idea of this work is that the quantum-classical isomorphism is a suitable framework for a generalization of the notion of detailed balance. The quantum-classical isomorphism is used in order to develop a Monte Carlo simulation with controlled deviation from detailed balance, that is with a generalized detailed balance and known relative entropy with respect to the reference process at each point. In order to apply this method to molecular simulations a new algorithm for realization of a partial chirotope, based on linear programming, a new distance geometry algorithm and a new all-atom off-lattice Monte Carlo method are proposed.

Keywords: Detailed balance; Distance geometry; Monte Carlo simulation; Quantum-classical isomorphism; Relative entropy
# Background

The characteristic time of an event in the molecular world is $10^{-15}$ sec, i.e. one iteration of a *molecular dynamics* must simulate changes corresponding to a time of this order. Biomolecules of interest, such as proteins, have thousands of atoms and, even using the simplest approximation for the molecular potential and a powerful computer, only thousand to million of iterations can be performed in a reasonable time. The approximate time of protein folding even in vivo is $10^{-5}$ sec. The timing for a standard Amber benchmark 159 residue protein in water is 249 ps/day of simulations on a single 3.4 GHz processor [2]. The performance of the NAMD program on different platforms can be viewed in [34]. However, significant changes of molecular conformations were achieved, for example, in all-atom molecular dynamics simulations of 36 residue protein on supercomputer of hundreds processors [11].

Another method of molecular simulation is molecular *Monte Carlo* simulation. It does not try to simulate the physical movement of a molecule but only visit (sample) its conformational space according to an appropriate probability distribution, such as Boltzmann distribution. It gives a hope of closing the aforementioned time gap.

A Monte Carlo (MC) simulation is a random process. Usually, it is a *Markov process* [19]. The Markov process $\{X_t\}_{t \in \mathbb{T}}$ is specified by its *transition probability* $P(s, x, t, Y) = P(X_t \in Y | X_s = x)$, $s \leq t$, and *initial distribution* - the distribution of the random variable $X_0$. $Y$ is in the smallest $\sigma$-algebra that contains all open sets of the state space $S$ of the process. If the transition probability depends only on the difference between $s$ and $t$, that is, if there exists a function $P(t, x, Y)$, such that $P(s, x, t, Y) = P(t - s, x, Y)$, then the Markov process is called *temporally homogeneous*. A *jump process* is a continuous time process which changes its state after non-zero time. A temporally homogeneous Markov jump process is determined by its initial distribution, jump rate $j(x)$ for a jump from each $x \in S$ and (jump) transition probability $P(x, Y)$ with (jump) transition probability density $p(x, y)$. Only temporally homogeneous Markov jump processes with $j(x) = 1$ for all $x \in S$
will be considered in this work. In this case jumps occur according to the Poisson process.

A process with the transition probability density \( p(x, y) \) satisfies the *semi-detailed balance condition* [13] if there exists a density \( \mu \) such that for all \( y \in S \)

\[
\int_{x \in S} \mu(x)p(x, y)dx = \mu(y).
\]

One says that such process with the initial density \( \mu \) is in a *steady state*.

A process with the transition probability density \( p(x, y) \) satisfies the *detailed balance condition* if there exists a density \( \mu \) such that for all \( x, y \in S \)

\[
\mu(x)p(x, y) = \mu(y)p(y, x).
\]

One says that such process with the initial density \( \mu \) is in *equilibrium*.

If a process with a finite number of states satisfies the detailed balance condition, then the process converges to a limiting distribution, which is unique [26], [30]. The simplest example of a process with detailed balance is a process with independent outcomes, that is \( p(x, y) = p(z, y) \) and \( \mu(x) = p(z, x) \) for all \( x, y, z \in S \).

A *Metropolis Monte Carlo* simulation [28] is an example of a process with detailed balance. Let given a system of particles in 3-dimensional space. Let \( r \) and \( n \) be vectors of coordinates of two states of the particle system in the phase space. The *Boltzmann law* gives the ratio of densities to be in the state \( r \) or \( n \) in equilibrium

\[
\frac{\mu(n)}{\mu(r)} = \exp\left(\frac{-(E(n) - E(r))}{kT}\right),
\]

where \( E(r) \) is the energy of the conformation of the particles, \( T \) is a temperature, \( k \) is the Boltzmann constant. The aim of the Metropolis MC sampling algorithm is to sample the phase space according to the distribution which satisfies the Boltzmann law. First, one generates a conformation \( r \) (present). Next, one generates a new conformation \( n \) by adding a small random displacement to \( r \). One must now decide whether the new conformation will be accepted or rejected. One wants to choose a
transition probability density $p(r, n)$ such that the detailed balance condition

$$\mu(r)p(r, n) = \mu(n)p(n, r)$$

is satisfied. We denote the probability density to try a move from $r$ to $n$ by $l(r, n)$ and the probability of accepting a move from $r$ to $n$ by $\alpha(r, n)$. Assume that the transition probability density is given by

$$p(r, n) = \alpha(r, n)l(r, n).$$

If $l$ is symmetric, i.e. $l(r, n) = l(n, r)$, then detailed balance implies

$$\mu(r)\alpha(r, n) = \mu(n)\alpha(n, r),$$

and therefore,

$$\frac{\alpha(r, n)}{\alpha(n, r)} = \exp\left(\frac{-(E(n) - E(r))}{kT}\right).$$

One of the possibilities to satisfy this condition is the choice of Metropolis et al. \[28\]

$$\alpha(r, n) = \min\{1, \exp\left(\frac{-(E(n) - E(r))}{kT}\right)\}.$$  

If $E(n) \leq E(r)$, then the move is accepted. If $E(n) > E(r)$, then we generate a random number $U$ from the uniform distribution in the interval $[0, 1]$ and we accept the move if $U < \alpha(r, n)$ and reject otherwise. $l$ is not specified, except for the assumption that it is symmetric. This reflects freedom in the choice of moves.

It is obvious that an infinite number of states of the gas corresponds to a given macroscopic condition of the gas. Through macroscopic measurements one should not be able to distinguish between two gases existing in different states (thus corresponding to two distinct representative points in phase space) but satisfying the same macroscopic conditions. Thus when one speaks of a gas under certain macroscopic conditions, one is in fact referring not to a single state, but to an infinite number of states. In other words, one refers not to a single system, but to a collection of systems, identical in composition and macroscopic condition but existing
in different states. Such a collection of systems is called an ensemble (Chapter 4 of [18]), which is geometrically represented by a distribution of representative points in phase space, usually a continuous distribution. An ensemble is completely specified by this distribution. Metropolis MC samples an ensemble which is called canonical ensemble. It is appropriate to a system whose temperature is determined through contact with a heat reservoir (Chapter 7 of [18]).

In generalized-ensemble simulations [33], each state is weighted by a non-Boltzmann probability weight factor. This allows the simulation to escape from energy barriers and to sample much wider space than by conventional methods. Monitoring the energy in a single simulation run in such ensembles, one can obtain also canonical ensemble averages as functions of temperature. One of the best-known generalized-ensemble methods is the replica-exchange MC [33],[35]. The system for a replica-exchange MC consists of non-interacting copies, or replicas, of the original system in canonical ensemble at different temperatures. There is a one-to-one correspondence between replicas and temperatures. A simulation of replica-exchange MC is then realized by alternately performing the following two steps.

1. each replica in the canonical ensemble at a fixed temperature is simulated simultaneously and independently for a certain number of Metropolis MC steps,

2. A random pair of replicas which are at neighboring temperatures \( T_m \) and \( T_{m+1} \) are exchanged moving the low-temperature conformation to the high-temperature simulation and vice versa. These replica swaps are accepted according to the Metropolis criterion with the acceptance probability

\[
\alpha_m = \min\{1, \exp\left(\frac{E_{m+1}}{kT_{m+1}} + \frac{E_m}{kT_m} - \frac{E_{m+1}}{kT_{m+1}} - \frac{E_m}{kT_m}\right)\}.
\]

The effect of replica exchange is to prevent low-temperature simulations from becoming trapped in local minima, because they are occasionally swapped to higher
temperatures where they can escape these minima and move to other regions of
phase space. Simultaneously, the low-temperature simulations are always being
seeded with low-energy conformations produced by simulations at higher tempar-
atures. The replica-exchange MC sampling is in detailed balance.

The notion of the quantum-classical isomorphism (sometimes it is called just the
classical isomorphism) originated in Chapter 10 of [12]. The derivation can be found
in Chapter 10 of [1]. Consider a quantum particle at temperature $T$, $\beta = 1/(kT)$. The density operator is $\rho = \exp(-\beta H)$, where $H = -\frac{p^2}{2m} + V(x)$. The density matrix is

$$\rho(r, r', \beta) = \langle r | \exp(-\beta H) | r' \rangle = \langle r | \exp(-\beta H/K) \ldots \exp(-\beta H/K) \ldots \exp(-\beta H/K) | r' \rangle.$$ 

Inserting unity in the form $1 = \int |r > < r | dr$ of the integral of projectors $|r > < r |$ over the volume of the system between each exponential gives

$$\rho(r, r', \beta) = \int < r | \exp(-\beta H/K) | r_2 > < r_2 | \exp(-\beta H/K) | r_3 > \ldots < r_{K-1} | \exp(-\beta H/K) | r_K > < r_K | \exp(-\beta H/K) | r' > dr_2 \ldots dr_K = \int \rho(r, r_2, \beta/K) \rho(r_2, r_3, \beta/K) \ldots \rho(r_K, r', \beta/K) dr_2 \ldots dr_K.$$ 

If $\beta/K$ is sufficiently small, the following approximation is valid [12]

$$\rho(r_a, r_b, \beta/K) \approx \rho_{\text{free}}(r_a, r_b, \beta/K) \exp \left(-\frac{\beta}{2K}(V^{cl}(r_a) + V^{cl}(r_b))\right)$$

where $V^{cl}(r)$ is the classical potential energy, and the free-particle density matrix for a single particle of mass $m$ is [12]

$$\rho_{\text{free}}(r_a, r_b, \beta/K) = \left(\frac{mK}{2\pi\beta\hbar^2}\right)^D \exp\left(-\frac{mK}{2\beta\hbar^2} r_{ab}^2\right),$$

where $r_{ab} = |r_a - r_b|$ and $D$ is a dimension of the space. Therefore

$$\rho(r_1, r_1, \beta) \approx \left(\frac{mK}{2\pi\beta\hbar^2}\right)^D \int \exp\left(-\frac{mK}{2\beta\hbar^2} (r_{12}^2 + r_{23}^2 + \ldots r_{K1}^2)\right)$$
\[ \exp \left( -\frac{\beta}{K} (V^d(r_1) + V^d(r_2) + \ldots V^d(r_K)) \right) dr_2 \ldots dr_K. \]  

The quantity \( \rho(r, r, \beta) \) is proportional to the density to be in \( r \). If an \( N \)-particle system is considered, replace \( D \) by \( ND \). That is, the density of the \( N \)-particle quantum system which satisfies the Boltzmann law corresponds to the density of the \( KN \)-particle classical system which satisfies the Boltzmann law and consists of \( K \) copies of the \( N \)-particle classical systems and in the copies with neighbor numbers \( i \) and \( i + 1 \) for \( 1 \leq i < K \) and \( K \) and 1 the corresponding particles are connected by springs with spring constant \( mK/(\beta^2\hbar^2) \). This approximation becomes exact as \( K \to \infty \) [1] and can be used in a conventional MC simulation to investigate quantum properties.

The main difficulties in all-atom detailed balanced MC simulations of biochemical processes involving big molecules are that these methods have huge autocorrelation time (Section 2 of [40]) and these processes, generally, do not approach to equilibrium.

A process is reversible if \( p(x, y) > 0 \) implies \( p(y, x) > 0 \) for all \( x, y \in S \). Let us mention some characteristics of non-equilibrium reversible processes. Such process satisfies the master equation

\[ \frac{d\mu_t(x)}{dt} = \int_{y \in S} \mu_t(y)p(y, x)dy - \mu_t(x). \]

For the probability density \( \mu_t \) the Gibbs entropy is given by

\[ S_G(\mu_t) = -\int_{x \in S} \mu_t(x) \log \mu_t(x) dx. \]

\( dS_G(\mu_t)/dt \) is deduced from master equation and according to Section 2.4 of [23] it splits into the entropy production rate \( R(\mu_t) \) and the entropy flow rate \( A(\mu_t) \) as follows

\[ \frac{dS_G(\mu_t)}{dt} = R(\mu_t) - A(\mu_t), \]

where

\[ R(\mu_t) = \frac{1}{2} \int \int_{x, y \in S} (\mu_t(x)p(x, y) - \mu_t(y)p(y, x)) \log \frac{\mu_t(x)p(x, y)}{\mu_t(y)p(y, x)} dxdy \]
\[ A(\mu_t) = \int_{x \in S} \mu_t(x) I(x) dx = \langle I \rangle_{\mu_t}, \]
\[ I(x) = \int_{y \in S} p(x, y) \log \frac{p(x, y)}{p(y, x)} dy. \]

The entropy production rate is expressed in Section 3.1 of [15] in terms of the "particle fluxes"
\[ J_t(x) = \mu_t(x)p(x, y) - \mu_t(y)p(y, x) \]
and "forces"
\[ F_t(x) = \log \frac{\mu_t(x)p(x, y)}{\mu_t(y)p(y, x)}. \]

As was mentioned in [6], entropy production rate can be considered as a measure of a lack of equilibrium.

**Definition 1.1 ([17])** For two probability distributions \( P \) and \( Q \) with probability densities \( p \) and \( q \), the relative entropy (Kullback-Leibler divergence) is defined by
\[ D_{KL}(P\|Q) = \int_{x \in S} p(x) \log \frac{p(x)}{q(x)} dx. \]
If entropy is measured in bits, the logarithm in this formula is taken to base 2, or to base \( e \), if entropy is measured in nats.

The Gibbs inequality says that \( D_{KL}(P\|Q) \geq 0 \) and the relative entropy is zero iff \( P = Q \). The entropy flow rate \( A(\mu_t) \) for the distribution \( \mu_t \) which is concentrated at one point \( x \) is the relative entropy of the transition probability density \( p'(y) = p(x, y) \) and the probability density \( p''(y) = p(y, x) \).

## 2 The problems addressed in this work

In this work we consider three different, but related problems:

1. generalizing the detailed balance condition in order to include processes which do not preserve any distribution, but with the property that, roughly speaking,
it is known how much information the "jumper" must retrieve from its path in order to reach its current position (when the corresponding reference process is given), then building processes with such generalized detailed balance,

2. enhancing all-atom off-lattice molecular MC simulations which are in detailed balance, for example replica-exchange MC, in order that they can be performed with a move set consisting of separate moves of each atom, with all degrees of freedom also in the case of dense atom packing; we do this by means of a new distance geometry algorithm, which plays in such MC simulations a role which is similar to the role of the SHAKE algorithm [36], [41] in molecular dynamics,

3. building an initial sample for all-atom off-lattice molecular MC simulations according to chirality constraints and distance constraints, and additionally, geometric manipulations with a molecule, which preserve, as far as possible, the aforementioned constraints, but exploit flexibility of a molecule.

The connecting link of the following considerations of these problems is the distance geometry procedure which we call "centering". We build an initial sample of a molecule satisfying molecular chirality constraints and distance constraints with the help of linear programming and subsequent "iterative vibrant centering". We perform a Metropolis MC with a move set consisting of separate moves of each atom in the sample space which is restricted with the help of "centering". We combine this distance geometry method and this MC to exploit flexibility of a molecule in geometric manipulations with it. We use the same restricted sample space in MC without detailed balance.

Section 3 provides an example of a process with generalized detailed balance with respect to its reference process using the quantum-classical isomorphism.

Section 4 provides the results of the numerical experiments considering some properties of the process which are similar to the example from Section 3, but can
be numerically examined.

Clearly, there is a temperature at which the Amber force field cannot ensure the integrity of the molecule in the all-atom Metropolis MC sampling with a move set consisting of separate moves of each atom as described in [28]. This limits replica temperatures in replica-exchange MC. The same phenomenon can happen in non-equilibrium simulations. A way to overcome this difficulty is to change the potential in order to restrict such deformations. We change the potential with the help of distance geometry “centering” procedure. It can be considered as building the restricted sample space which includes all relevant conformations. It is described in Section 5.

In order to start a Metropolis MC with this potential one has to build an initial sample which is in the restricted sample space. As will be proved in Section 6, if one starts at some point of the sample space and performs as many centerings as needed from an infinite sequence of centerings which contains an infinite number of centerings of each atom, then at certain step one reaches a point in the aforementioned restricted sample space. We call this algorithm “iterative centering”.

Molecular chirality constraints impose limitations on molecular conformations. These limitations are in addition to the limitations imposed by the weighted graph of the desired distances. A new algorithm for realization of a partial chirotope, based on linear programming is proposed in Section 7.

Suppose, that a sample which satisfies a given partial chirotope (chirality constraints) is built. Now we need to push this sample into the restricted sample space. Numerical tests show, that reiteration of iterative centering algorithm with chirality checking can become jammed if the initial sample is far from the restricted sample space. For overcoming this difficulty the “vibrant iterative centering” distance geometry algorithm is proposed in Section 8. The vibrant iterative centering algorithm can be incorporated in a convenient computation scheme with a Metropolis MC in the restricted sample space. This scheme allows flexible manipulations with
a molecule with further equilibration. It is described in Section 8.

Section 9 describes a molecular MC simulation without detailed balance using the quantum-classical isomorphism. In this simulation we use a process which is similar to the example which is described in Section 3. The simulation of Section 9 is only preliminary since the choice of appropriate parameters for true molecular simulations is not considered in this work, but the observations of Section 9 hints at the possibility to use such method in molecular MC.

All algorithms with centerings are new. The iterative vibrant centering can be useful in existing distance geometry software in order to improve its sampling properties. The restricted sample space can be useful in all-atom off-lattice molecular simulation software, for example, in order to increase the temperature of the hottest replica in replica-exchange MC. The algorithm for realization of a partial chiro-tope using linear programming is also new. It can be useful with iterative vibrant centering.

The notion of generalized detailed balance in a framework of Langevin dynamics was proposed in [21]. As far as we know, our work is the first attempt to generalize the detailed balance condition in order to include processes which are not in a steady state but with the property, that it is known how much information the jumper must retrieve from its path in order to reach its current position (when the corresponding reference process is given). In our opinion the appropriate generalization of the detailed balance condition is the most important problem in computer molecular simulations, since we believe that an all-atom detailed balanced simulation of working ribosome will never be possible on a digital computer.

The concepts of vertex, particle, bead and atom represent the same object in different contexts of this work. The notations of Sections 5, 6, 7, 8 are independent of the notations of Sections 1, 3, 4, 9.
3 Generalized detailed balance

Consider the Young’s double-slit experiment (§§26,27,32,33 of [25]). Let two parallel plane screens be separated by a distance $l$. Let there be $N \geq 1$ rectilinear parallel slits of width $s$ on the first screen. In the case of the Young’s double-slit experiment $N = 2$. Let the correspondent slit borders of neighbor slits be separated by a distance $d$. Let there be a plane monochromatic light wave with length $\lambda$ which propagates perpendicularly to the screens and hits the second screen through the slits in the first screen. If $\lambda \ll s \leq d \ll l$, then the intensity on the second screen is

$$I(y) = I_0 \frac{\sin^2 Y \sin^2(NqY)}{N^2 Y^2 \sin^2(qY)},$$

where $y$ is a distance between a point on the second screen and perpendicular projections of the slits on the second screen,

$$Y = \frac{\pi s}{\lambda} y,$$

$q = d/s \geq 1$ and $I_0$ is the maximum intensity on the second screen. In this case the Fraunhofer diffraction takes place, that is $I(ly_1)/I(ly_2)$ does not depend on $l$.

Since

$$\int_0^\infty \frac{\sin^2(ax)}{x^2} dx = |a| \frac{\pi}{2},$$

(3.821.9 from [16]), without loss of generality let the intensity distribution for $N = 1$ be

$$I_1(x) = \frac{\sin^2 x}{\pi x^2}.$$

Since

$$\int_0^\infty \frac{\sin^2(ax) \cos^2(bx)}{x^2} dx = \frac{a\pi}{4},$$

for $0 < a \leq b$ (3.828.11 from [16]), let the intensity distribution for $N = 2$ be

$$I_2(x) = \frac{\sin^2 x \sin^2(2qx)}{2\pi x^2 \sin^2(qx)}.$$

Then

$$\int_{-\infty}^{\infty} I_1(x) \log_2 \frac{I_1(x)}{I_2(x)} dx = 1.$$
since
\[ \int_0^\infty \frac{\log \cos^2(ax)}{x^2} \cos(bx) \, dx = -a\pi + \pi b \log 2 + \pi \sum_{n=1}^m \frac{(-1)^n(b - 2an)}{n}, \]
where \( m \leq b/(2a) < m + 1, m = 0, 1, 2, 3, \ldots \) (I.158 from [32]).

In this example 1 bit of the information through what slit the photon passed translates in 1 bit of relative entropy \( D_{KL}(I_1(x)\|I_2(x)) \) for all \( q = d/s \geq 1 \). The process ”without information” can be considered as a reference process. The formula for Fraunhofer diffraction is an approximation, but this property can be directly verified in experiments on various screens. We call this property by the balance of relative entropy.

In the path integral formulation of quantum mechanics [12] the contribution of a particular path in the total probability amplitude for a photon has a phase proportional to time to travel along this path. In the aforementioned example the contribution of a particular path changes along this path such that the total intensity obeys the property of balanced relative entropy. A time with such property ”rotates” in order to hide the information about the past which was not retrieved in time.

The rest of this section is devoted to giving an example of the process with jumps which obey the property of balanced relative entropy. If the reference process is in detailed balance, then the condition of the balance of relative entropy can be considered as a generalization of the detailed balance condition.

In order that the quantum-classical isomorphism be valid, the Boltzmann law must be satisfied [12]. Therefore MC with independent outcomes of one quantum particle using the quantum-classical isomorphism with condition, that the vector of the coordinates \( a_0 \) of the first copy of the particle is in the zero point must be defined by the following recurrent Levy construction [24] for \( 1 \leq n < K \)

\[ a_n = \frac{K-n}{K-n+1}a_{n-1} + \frac{1}{\sqrt{\frac{mK}{\hbar e} (1 + \frac{1}{K-n})}} \eta_n \quad (2) \]

where each \( \eta_n \) is a vector with independent standard normal distributed coordinates. The Levy construction samples intermediate time points of a Brownian mo-
tion, conditioned to arrive to a predetermined point after a predetermined time. A
Brownian bridge is a Brownian motion conditioned to return to the initial point
after a predetermined time. The aforementioned MC sample \((a_0, \ldots, a_{K-1})\) is the
Levy construction for a Brownian bridge for the time interval divided into \(K\) equal
subintervals with \(a_0 = 0\). In the case of the quantum-classical isomorphism, this
Brownian bridge time parameter is considered as “imaginary time” \(^{12}\) in contrast
with ordinary time where the jumps of MC take place. In this work, imaginary
time is discrete and denoted by a subscript and ordinary time is continuous, but a
number of jumps in jump processes is denoted by a superscript.

Consider MC simulations of two distinguishable quantum particles. Firstly we
define an auxiliary process \(\{N_t\}\).

Let \((a_0, \ldots, a_{K-1})\) and \((b_0, \ldots, b_{K-1})\) be the aforementioned Levy constructions
with \(a_0 = 0\) and \(b_0 = 0\). Shift them by \(a\) and \(b\) according to the distribution
of \(N_0\), that is \((a_{1}^{1}, \ldots, a_{K-1}^{1}) = (a_0, \ldots, a_{K-1}) + (a, \ldots, a)\) and \((b_{0}^{1}, \ldots, b_{K-1}^{1}) =
(b_0, \ldots, b_{K-1}) + (b, \ldots, b)\). This is an initial sample for \(\{N_t\}\).

Suppose, that \(i\) samples of \(\{N_t\}\) are built, that is \(i-1\) jumps of \(\{N_t\}\) have
already happened. Build new Levy constructions \((\hat{a}_{0}^{i}, \ldots, \hat{a}_{K-1}^{i})\) and \((\hat{b}_{0}^{i}, \ldots, \hat{b}_{K-1}^{i})\).
Randomly choose two numbers \(n_1^i\) and \(n_2^i\), \(n_1^i < n_2^i\), from 0 to \(K-1\) with equal
probability for each pair. If

\[
\|a_{n_1^i}^i - b_{n_2^i}^i\| < \|a_{n_2^i}^i - b_{n_1^i}^i\| \tag{3}
\]

shift these new Levy constructions \((\hat{a}_{0}^{i}, \ldots, \hat{a}_{K-1}^{i})\) and \((\hat{b}_{0}^{i}, \ldots, \hat{b}_{K-1}^{i})\) by \(a_{n_1^i}^i - \hat{a}_{n_1^i}^i\)
and \(b_{n_2^i}^i - \hat{b}_{n_2^i}^i\) correspondingly with probability \(\alpha\), otherwise, shift them by \(a_{n_2^i}^i - \hat{a}_{n_2^i}^i\)
and \(b_{n_1^i}^i - \hat{b}_{n_1^i}^i\). If \(\|a_{n_1^i}^i - b_{n_1^i}^i\| > \|a_{n_2^i}^i - b_{n_2^i}^i\|\) shift them by \(a_{n_2^i}^i - \hat{a}_{n_2^i}^i\) and \(b_{n_1^i}^i - \hat{b}_{n_1^i}^i\)
with probability \(\alpha\), otherwise, shift them by \(a_{n_1^i}^i - \hat{a}_{n_1^i}^i\) and \(b_{n_2^i}^i - \hat{b}_{n_2^i}^i\)
and so on.

\(\{N_t\}\) satisfies (1) if it is in a steady state. Denote \(\{N_t\}\) with \(\alpha = 1\) by \(\{M_t\}\)
and denote \(\{N_t\}\) with \(\alpha = 1/2\) by \(\{L_t\}\). The process \(\{L_t\}\) is a well-known MC
of two free particles using quantum-classical isomorphism. Jumps of \(\{M_t\}\) satisfies
the balanced relative entropy condition with respect to jumps of \(\{L_t\}\). Now, given
4 Numerical experiments

In order to present the results of the numerical experiments, we define some processes which are similar to \( \{ N_t \} \). All these processes consider \( K \) copies of two particles in \( \mathbb{R} \). The copies are connected by springs as described in the discussion of the quantum-classical isomorphism in Section 1. The first sample for all the processes of this section is \(((0,\ldots,0),(\delta,\ldots,\delta))\), where \( \delta > 0 \) is large relative to the lengths of the steps of the processes.

Define \( \{ N^j_i \} \) for \( 0 < j < K \) as follows. Suppose, that \( i \) samples of \( \{ N^j_i \} \) are built. Build new Levy constructions \((\hat{a}_0^i,\ldots,\hat{a}_{K-1}^i)\) and \((\hat{b}_0^i,\ldots,\hat{b}_{K-1}^i)\) according to (2). Randomly choose a number \( n_1^i \) from 0 to \( K - 1 \) with equal probability for each number. Let \( n_2^i \equiv n_1^i + j \mod K \). If \( ||\hat{a}_{n_1^i}^i - b_{n_2^i}^i|| < ||\hat{a}_{n_2^i}^i - b_{n_1^i}^i|| \) shift these Levy constructions \((\hat{a}_0^i,\ldots,\hat{a}_{K-1}^i)\) and \((\hat{b}_0^i,\ldots,\hat{b}_{K-1}^i)\) by \( \hat{a}_{n_1^i}^i - \hat{a}_{n_2^i}^i \) and \( \hat{b}_{n_2^i}^i - \hat{b}_{n_1^i}^i \) correspondingly with probability \( \alpha \) (these jumps we call ”forward jumps”) otherwise shift them by \( \hat{a}_{n_2^i}^i - \hat{a}_{n_1^i}^i \) and \( \hat{b}_{n_1^i}^i - \hat{b}_{n_2^i}^i \) (”backward jumps”). If \( ||\hat{a}_{n_1^i}^i - b_{n_2^i}^i|| > ||\hat{a}_{n_2^i}^i - b_{n_1^i}^i|| \) shift them by \( \hat{a}_{n_2^i}^i - \hat{a}_{n_1^i}^i \) and \( \hat{b}_{n_1^i}^i - \hat{b}_{n_2^i}^i \) with probability \( \alpha \) (”forward”) otherwise shift them by \( \hat{a}_{n_1^i}^i - \hat{a}_{n_2^i}^i \) and \( \hat{b}_{n_2^i}^i - \hat{b}_{n_1^i}^i \) (”backward”) and so on.

Define \( \{ W^j_i \} \) for \( 0 < j < K \) as follows. Suppose, that \( i \) samples of \( \{ W^j_i \} \) are built. Randomly choose a number \( n_1^i \) from 0 to \( K - 1 \) with equal probability for each number. Let \( n_2^i \equiv n_1^i + j \mod K \) and \( h_q = mK/(\beta^2\hbar^2) \).

If \( ||\hat{a}_{n_1^i}^i - b_{n_2^i}^i|| < ||\hat{a}_{n_2^i}^i - b_{n_1^i}^i|| \), then with probability \( \alpha \)

\[
\begin{align*}
\hat{a}_{n_2^i}^{i+1} &= \frac{a_{n_2^i}^i + a_{n_2^i+1}^i}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta_i, \\
\hat{b}_{n_2^i}^{i+1} &= \frac{b_{n_2^i}^i + b_{n_2^i+1}^i}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta'_i
\end{align*}
\]
and other coordinates unchanged, otherwise

\[ a_{n_1}^{i+1} = \frac{a_{n_1}^i + a_{n_1}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta_i, \quad b_{n_2}^{i+1} = \frac{b_{n_2}^i + b_{n_2}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta'_i \]

and other coordinates unchanged.

If \( \|a_{n_1}^i - b_{n_1}^i\| > \|a_{n_2}^i - b_{n_2}^i\| \), then with probability \( \alpha \)

\[ a_{n_1}^{i+1} = \frac{a_{n_1}^i + a_{n_1}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta_i, \quad b_{n_2}^{i+1} = \frac{b_{n_2}^i + b_{n_2}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta'_i \]

and other coordinates unchanged, otherwise

\[ a_{n_2}^{i+1} = \frac{a_{n_2}^i + a_{n_2}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta_i, \quad b_{n_1}^{i+1} = \frac{b_{n_1}^i + b_{n_1}^{i+1}}{2} + \frac{1}{\sqrt{2\beta h_q}} \eta'_i \]

and other coordinates unchanged.

The following numerical experiments show that in some sense \( \{W_i^j\} \) and \( \{N_i^j\} \) are similar. Consider \( K = 8, 16, 32, 64, 128, \alpha = 1, 2/3, 7/12, 13/24, 25/48 \). Let \( m \) be atomic mass unit, \( T = 300K \). Standard normal distributed random numbers are obtained by the Box-Muller algorithm \[10\] from the uniformly distributed pseudo-random numbers \[27\]. We compute the following quantities: the number of performed jumps \( J \), the number \( F \) of forward jumps \( i \leq J \) for which \( \|a_{n_1}^i - b_{n_1}^i\| - \|a_{n_2}^i - b_{n_2}^i\| \) and \( \|a_{n_1}^{i+1} - b_{n_1}^{i+1}\| - \|a_{n_2}^{i+1} - b_{n_2}^{i+1}\| \) have different signs, the number of such backward jumps \( R \), the average of the coordinates \( A = \frac{1}{K} \sum_{n=1}^{K} a_n^{j+1} \) after the last jump, the average \( B = \frac{1}{K} \sum_{n=1}^{K} (b_n^{j+1} - \delta) \), the average number \( C = \frac{1}{K} \sum_{n=1}^{K} C_n \), where \( C_n \) is the number of \( i \leq J \) such that \( \|a_n^i - b_n^i\| - \|a_n^{i+1} - b_n^{i+1}\| \) and \( \|a_n^{i+1} - b_n^{i+1}\| - \|a_n^{i+1} - b_n^{i+1}\| \) have different signs, where \( n' \equiv n + j \) (mod \( K \), \( A + B \)) \( \frac{\sqrt{K}}{F - K} \) and \( \frac{(A + B) \sqrt{K}}{(F - K) C} \).

The results for \( \{N_i^j\} \) are shown in Table \[1\] of Appendix, the results for \( \{W_i^j\} \) are shown in Table \[2\] of Appendix. In the case of \( \{N_i^j\} \) we take \( J / C = 2 \). The lengths in these tables are in units \( \frac{h}{\sqrt{mkT}} \). The observations are as follows.

1. For both \( \{N_i^j\} \) and \( \{W_i^j\} \), if we fix \( K \) and \( j \), then \( A \) and \( B \) are proportional to \( \alpha - 1/2 \).
2. For \( \{W_i^j\} \), if we fix \( K \), then \( \frac{A+R}{\mathcal{J}} \) is approximately constant. It is true also when \( j \) is not a constant, but a random variable, for example, uniformly distributed in some interval, as for \( \{N_t\} \) (Not shown in the Appendix).

3. If we fix \( j/K \), the closeness of \( \frac{(A+R)}{\mathcal{J}} \) for \( \{N_t^j\} \) and for \( \{W_t^j\} \) justifies that \( \mathcal{J}/\mathcal{C} \) jumps of \( \{W_t^j\} \) approximate two jumps of \( \{N_t^j\} \).

5 The restricted sample space

Evidently, there is a temperature at which the Amber force field cannot ensure the integrity of the considered molecule in the all-atom Metropolis MC sampling with the move set consisting of the separate moves of each atom as described in \[28\]. This limits replica temperatures in the replica-exchange MC. The same phenomenon can happen in non-equilibrium simulations. A way to overcome this difficulty is to change the potential in order to restrain such deformations.

A finite undirected weighted graph \( G \) is a triple \( < V, E, W > \), where \( V \) denotes the set of its vertices, \( E \) denotes the set of its edges, and \( W : E \rightarrow \mathbb{R}^+ \) is a function which specifies a positive weight for each graph edge. In order to restrict the sample space as was mentioned in Section \[2\] one has to set a weighted graph which corresponds to the molecule. Generally, atoms are vertices of this graph, covalent bonds form a part of its edges, pairs of atoms which are bonded through two covalent bonds form another part of its edges, weights are desired distances. The weights of edges which connect two atoms which are bonded through two covalent bonds determine the bond angles. So, the weighted graph of methane has 10 undirected weighted edges. The weighted graph of amide plane has also \( C^\alpha - C^\alpha \) and \( H - O \) edges, since their distances are well defined in amide plane. If one knows additional distances between atoms (for example from Nuclear Magnetic Resonance data), one adds corresponding edges and weights too.

Let \( f : V \rightarrow \mathbb{R}^k \) be a conformation of \( G \) in the \( k \)-dimensional Euclidean space \( \mathbb{R}^k \)
(regardless of the weights). Let the coordinates of vertices $a_v = f(v)$ be all distinct and let $h : E \to \mathbb{R}^+$ be the spring constants of edges. The point 

$$c_u = \frac{1}{\sum_{\{v\mid \{u,v\} \in E\}} h(\{u,v\})} \sum_{\{v\mid \{u,v\} \in E\}} h(\{u,v\}) \left( a_v + \frac{W(\{u,v\})}{\|a_u - a_v\|} (a_u - a_v) \right)$$

(4)

will be called the center of the vertex (atom) $u$.

The corresponding algorithm for finding the center of the vertex $u$ takes as its input the adjacency-list representation \[8\] of the finite weighted graph $G = < V, E, W >$ and current coordinates of its vertices. The adjacency-list representation of the graph consists of the array $Adj$ of $|V|$ lists, one for each vertex in $V$. For each $u \in V$ the adjacency list $Adj[u]$ contains all the vertices $v \in V$ such that there exists an edge $\{u, v\} \in E$. The weight $W(\{u, v\})$ of the edge $\{u, v\} \in E$ is stored with a vertex $v$ in $u$’s adjacency list. $h(\{u,v\})$ are stored like $W(\{u,v\})$ and the vector $A[u]$ of current coordinates of the vertex $u$ is stored with $u$. If $x$ is a pointer to an element of the list $Adj[u]$, then, according to pseudocode conventions \[8\], $\text{vertex}[x]$ denotes a vertex which adjacent to $u$ ( denote it by $v$ ), $W[x]$ and $H[x]$ denote $W(\{u,v\})$ and $h(\{u,v\})$.

```
Center(u)
1    t ← 0
2    q ← 0
3    y ← (0, 0, 0)
4    f ← 0
5    x ← head(Adj[u])
6    while x ≠ NIL
7        do   v ← vertex[x]
8            z ← A[u] - A[v]
9            r ← ||z||
10           if $r > 0$
11              then $y ← y + H[x](A[v] + (W[x]/r)z)$
```
As will be proved in Section 6, if one starts at arbitrary point of a sample space and performs as many centerings as needed from a sequence of centerings which contains an infinite number of centerings of each vertex, then at some step one achieves a point of a sample space such that for each \( u \in V \) it holds that \( \|a_u - c_u\| < S(u) \) for a given \( S(u) > 0 \). Denote the set of such points by \( \mathcal{D}(S) \). As will be viewed in Section 6 the Hooke potential \( \sum_{e \in E} \frac{h(e)}{2} (\|e\| - W(e))^2 \) is large outside \( \mathcal{D}(S) \). We change a given potential, for example the Amber force field, by assuming it infinitely large outside of \( \mathcal{D}(S) \). \( S(u) \) has to be not too small if one does not want to restrict a considerable part of molecular degrees of freedom.

6 The iterative centering algorithm

Distance geometry is a part of computational geometry which is devoted to the study of the existence or non-existence of an embedding satisfying the condition in
the following definition as well as methods for construction of such embedding.

**Definition 6.1** Let $G = \langle V, E, W \rangle$ be a finite undirected weighted graph, where $V$ denotes the set of its vertices, $E$ denotes the set of its edges, and $W : E \to \mathbb{R}^+$ is a function which specifies a positive weight for each graph edge. An embedding of $G$ in the $k$-dimensional Euclidean space $\mathbb{R}^k$ is a function $f : V \to \mathbb{R}^k$ such that for each edge $e = \{v, w\} \in E$ one has $\|f(v) - f(w)\| = W(e)$. $G$ is called $k$-embeddable iff such an embedding exists.

The problem of $k$-Embeddability of an integer-weighted undirected graph is NP-hard [37]. However there is a semidefinite programming algorithm for the Euclidean distance matrix completion problem, i.e. determining whether there exists a number $k$ for which a given undirected weighted graph is $k$-embeddable [22]. If there exists an embedding according to Definition 6.1 it is evidently in $\mathcal{D}(S)$.

**Theorem 6.2 ([4])** A complete graph is $k$-embeddable iff each of its complete subgraphs with $k + 3$ vertices is $k$-embeddable.

Another distance geometry problem is that of bounded $k$-Embeddability, namely whether for given bounds $l, u : E \to \mathbb{R}^+$ there exists a weight $W$ with $l(e) \leq W(e) \leq u(e)$ for which a graph $G = \langle V, E, W \rangle$ is $k$-embeddable.

There are number of methods which can be applied to solving the aforementioned problems, which generally arise in Nuclear Magnetic Resonance data interpretation: **metric matrix distance geometry** [9, 31], **simulated annealing**, **variable target function optimization** [7] and **global continuation** [29].

The **iterative centering** distance geometry algorithm consists of performing as many steps as needed from an infinite sequence of centerings which contains an infinite number of centerings of each vertex.

**Proposition 6.3** Let $\{u_k\}$ be an infinite sequence of vertices of $G$. Let us apply a sequence $\{\text{Center}(u_k)\}_{1 \leq k \leq n}$ of $n$ centerings. Denote the displacement of the vertex $u_n$ after the iteration $\text{Center}(u_n)$ by $l_n$. Then $\lim_{n \to \infty} \|l_n\| = 0$. 
Proof. Without loss of generality suppose that all coordinates of \( u_n \) after \( n - 1 \) iterations are zero. Denote the coordinate vectors of vertices adjacent to \( u_n \) after \( n - 1 \) iterations by \( a_1, \ldots, a_m \), the corresponding weights by \( w_1, \ldots, w_m \) and the spring constants by \( h_1, \ldots, h_m > 0 \). If \( \| a_i \| > 0 \) for every \( i, 1 \leq i \leq m \), then according to (4) the coordinates of \( u_n \) after \( n \) iterations is

\[
y = \frac{1}{\sum_{i=1}^{m} h_i} \sum_{i=1}^{m} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i.
\]

Therefore

\[
\left( \sum_{i=1}^{m} h_i \right) \| y \|^2 = \sum_{i=1}^{m} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) \| a_i \|^2 - \sum_{i=1}^{m} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i - y \|^2
\]

similar to the Huygens theorem about momenta.

\[
\left\| \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i - y \right\| \geq \left\| a_i - y \right\| - w_i
\]

by the triangle inequality and

\[
\left\| \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i \right\| = \left\| a_i \right\| - w_i.
\]

Therefore

\[
\left( \sum_{i=1}^{m} h_i \right) \| y \|^2 \leq \sum_{i=1}^{m} h_i (\| a_i \| - w_i)^2 - \sum_{i=1}^{m} h_i (\| a_i - y \| - w_i)^2.
\]

(5)

If \( \| a_i \| > 0 \) for every \( i, 1 \leq i \leq k \), and \( \| a_i \| = 0 \) for every \( i, k + 1 \leq i \leq m \), we take some \( z, \| z \| = 1 \) and we define

\[
y = \frac{1}{\sum_{i=1}^{k} h_i} \left( \sum_{i=1}^{k} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i + \sum_{i=k+1}^{m} h_i w_i z \right).
\]

Similarly to the previous, we have (5). We put

\[
z = \frac{1}{\sum_{i=1}^{k} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i} \sum_{i=1}^{k} h_i \left( 1 - \frac{w_i}{\| a_i \|} \right) a_i
\]

as in the Center(\( u \)) algorithm. The right hand side of (5) is twice the difference of the old and the new values of the Hooke potential \( \sum_{e \in E} \frac{k(e)}{2}(\| e \| - W(e))^2 \). That
is, at stage $n$, the Hooke potential decreases by at least $\left( \sum_{i=1}^{m} h_i \right) \| l_n \|^2$, where $l_n$ is the shift of the center. If $\| l_n \| \not\to 0$, then the Hooke potential would become negative at some $n$. Since Hooke potential is non-negative we have $\lim_{n \to \infty} \| l_n \| = 0$. □

7 The realization of the partial chirotope related to the molecular chirality constraints

Let $x_1, x_2, \ldots, x_r, y_1, y_2, \ldots, y_r \in \mathbb{R}^r$. Then the following Grassmann-Plucker relation holds

$$\det(x_1, x_2, \ldots, x_r) \cdot \det(y_1, y_2, \ldots, y_r) = \sum_{i=1}^{r} \det(y_i, x_2, \ldots, x_r) \cdot \det(y_1, \ldots, y_{i-1}, x_1, y_{i+1}, \ldots, y_r).$$

The difference of the left and the right sides is an alternating multi-linear form in the $r+1$ arguments $x_1, y_1, y_2, \ldots, y_r$, which are vectors in an $r$-dimensional vector space; hence, the difference of the left and the right sides is identically zero. For example, in rank 3 one gets for every set of 5 vectors (denoting determinants by square brackets, and labeling the points 1 to 5) the relation $[123][145] - [124][135] + [125][134] = 0$. This requires that these 6 signs of the brackets on the left side are such that the equality is at least possible for this sign pattern, when actual scalars are not given: for example, these 6 signs could be $++,+,+,+,+,+$, but not $+,+,+,+,+,+$.

Definition 7.1 ([3]) Let $r \geq 1$ be an integer, and let $E$ be a finite set. A chirotope of rank $r$ on $E$ is a mapping $\chi : E^r \to \{ -1, 0, 1 \}$ which satisfies the following 3 properties:

1. $\chi$ is not identically 0,

2. $\chi$ is alternating, that is, $\chi(a_{\sigma_1}, a_{\sigma_2}, \ldots, a_{\sigma_r}) = \text{sign}(\sigma) \chi(a_1, a_2, \ldots, a_r)$ for all $a_1, a_2, \ldots, a_r \in E$ and every permutation $\sigma$,
3. for all \(a_1, a_2, \ldots, a_r, b_1, b_2, \ldots, b_r \in E\) such that
\[
\chi(a_1, a_2, \ldots, a_r) \cdot \chi(b_1, b_2, \ldots, b_r) \neq 0,
\]
there exists an \(i \in \{1, 2, \ldots, r\}\) such that
\[
\chi(b_i, a_2, \ldots, a_r) \cdot \chi(b_1, \ldots, b_{i-1}, a_1, b_{i+1}, \ldots, b_r) = \chi(a_1, a_2, \ldots, a_r) \cdot \chi(b_1, b_2, \ldots, b_r).
\]

The axioms come from abstracting sign properties in the Grassmann-Plucker relations for \(r\)-order determinants. The chirotope axioms are a version of the oriented matroid axioms.

Suppose \(E = \{1, 2, \ldots, n\}\). Given any \((n - r)\)-tuple \((a_1, \ldots, a_{n-r})\) of elements in \(E\), then we write \((a'_1, \ldots, a'_r)\) for some permutation of \(E \setminus \{a_1, \ldots, a_{n-r}\}\). Then \((a_1, \ldots, a_{n-r}, a'_1, \ldots, a'_r)\) is a permutation of \((1, 2, \ldots, n)\), and we can compute
\[
\text{sign}(a_1, \ldots, a_{n-r}, a'_1, \ldots, a'_r)
\]
as the parity of the number of inversions of this string. The mapping \(\chi^* : E^{n-r} \to \{-1, 0, 1\}\), defined by
\[
\chi^*(a_1, \ldots, a_{n-r}) = \chi(a'_1, \ldots, a'_r) \text{sign}(a_1, \ldots, a_{n-r}, a'_1, \ldots, a'_r)
\]
is called the chirotope dual to the chirotope \(\chi\).

Let \(\chi : E^r \to \{-1, 0, 1\}\) be a chirotope, \(E = \{1, \ldots, n\}\). If there exists \(\{x_1, \ldots, x_n\} \subset \mathbb{R}^r\) such that
\[
\chi(a_1, a_2, \ldots, a_r) = \text{sign}(\det(x_{a_1}, x_{a_2}, \ldots, x_{a_r}))
\]
for all \(1 \leq a_1 < a_2 < \ldots < a_r \leq n\), then \(\chi\) is called realizable and \(q : E \to \mathbb{R}^r, i \mapsto x_i\) is called a realization of \(\chi\).

Let \(G_r(\mathbb{R}^n)\) be the real Grassmann manifold of \(r\)-dimensional linear subspaces in \(\mathbb{R}^n\), or equivalently \(\text{Mat}_{r \times n}(\mathbb{R})/\text{GL}_r(\mathbb{R})\), which corresponds to the space of configurations of \(n\) vectors in \(\mathbb{R}^r\) modulo the action of the general linear group \(\text{GL}_r(\mathbb{R})\). Thus the realization \(q\) of \(\chi\) corresponds to a point in \(G_r(\mathbb{R}^n)\). The set of such points is called the realization space of \(\chi\).
Let \( \chi : E^r \to \{-1, 0, 1\} \) be a chirotope. Then for each subset \( \{a_1, \ldots, a_{r+2}\} \) of \( E \) there exists \( \{x_1, \ldots, x_{r+2}\} \subset \mathbb{R}^r \) such that
\[
\chi(a_{i_1}, a_{i_2}, \ldots, a_{i_r}) = \text{sign}(\det(x_{i_1}, x_{i_2}, \ldots, x_{i_r}))
\]
for all \( 1 \leq i_1 < i_2 < \ldots < i_r \leq r + 2 \). This feature of chirotopes is called by local realizability. Local realizability follows from the facts that realizability is preserved under duality since \( G_r(\mathbb{R}^n) = G_{n-r}(\mathbb{R}^n) \) and that all rank 2 chirotopes are realizable.

The realizability problem for chirotopes is NP-hard [3]. There is an algorithm for a realization of a chirotope \( \chi \) which is valid when the realization space of \( \chi \) is contractible and \( \chi : E^r \to \{-1, 1\} \) [5], [9].

If the alternating map \( \chi \) is only partially defined and the Grassmann-Plucker relation holds whenever \( \chi \) is defined on all its participants, then \( \chi \) is called a partial chirotope. A partial chirotope \( \chi' \) of rank \( r \) on \( E \) is called extendable if there exists a chirotope \( \chi \) of rank \( r \) on \( E \) and for any \( a_1, \ldots, a_r \in E \), \( \chi'(a_1, \ldots, a_r) = \chi(a_1, \ldots, a_r) \) holds whenever \( \chi'(a_1, \ldots, a_r) \) is defined. The problem of testing extendability of a partial chirotope is NP-complete [42].

Molecular chirality constraints impose limitations on molecular conformations. These limitations are in addition to the limitations imposed by weighted graph of desired distances. A set of inequalities of type \( \det(x_b - x_a, x_c - x_a, x_d - x_a) > 0 \), where \( a, b, c, d \in V \), corresponds to molecular chirality constraints. Then the corresponding equalities \( \chi(a, b, c, d) = 1 \) define a rank 4 partial chirotope. If \( a \mapsto (x^1_a, x^2_a, x^3_a) \) satisfies these inequalities, then \( a \mapsto (1, x^1_a, x^2_a, x^3_a) \) is a realization of the corresponding partial chirotope. The most widely adopted method to realize a partial chirotope related to molecular chirality constraints is the minimization of the function, which includes deviations from given oriented volumes, by simulated annealing starting from an approximate embedding [31]. An example of a realization of a partial chirotope by use of such function can be found in [33].

Let "maximize \( cx \) with conditions \( Ax \leq b \) and \( x \geq 0 \)" be a linear program. \( x \geq 0 \) means \( x_j \geq 0 \) for all \( j \). Particularly, let \( c_j \) be the price per unit of the product \( j \).
produced, $x_j$ be the quantity of the product $j$ produced, $b_i$ be the quantity of the material $i$ on hand, $a_{ij}$ be the quantity of the material $i$ required to produce one unit of the product $j$. Let $y_i$ be the price per unit of the material $i$. One is interested in selling the materials instead of the products if $A^T y \geq c$. The dual linear program "minimize by $y$ with conditions $A^T y \geq c$ and $y \geq 0"$ answers the question what is the minimal price of all materials when it is advantageous to sell the materials instead of to work. This price is the same as the maximal income in the first (primal) linear program. It is the figurative formulation of the linear programming strong duality theorem as economists learn it.

In some cases the following algorithm allows one to realize a given molecular partial chirotope. Let $Y \subset V$ be a set of vertices, whose coordinates appear in inequalities of type $\det(x_b - x_a, x_c - x_a, x_d - x_a) > 0$. Without loss of generality one can demand $\det(x_b - x_a, x_c - x_a, x_d - x_a) \geq \epsilon > 0$ for all these inequalities and $z_i = x_i^3 \geq 0$ for all $i \in Y$. If we fix $x_i^1$ and $x_i^2$ for all $i \in Y$ then the inequalities become linear. A feasible solution of the following (symmetric) linear programming problem

$$\text{Minimize } z_1 + \ldots + z_m \text{ subject to } Az \geq \epsilon \text{ and } z \geq 0$$

is a solution of our problem. Its dual problem

$$\text{Maximize } \epsilon t_1 + \ldots + \epsilon t_k \text{ subject to } A^T t \leq 1 \text{ and } t \geq 0$$

has zero as a feasible solution. If the original problem has a feasible solution, then its dual is bounded by the strong duality theorem. The dual problem can be solved by the primal simplex procedure and if it is bounded, then the solution of the original problem can be taken from the last simplex tableau, according to the Chapter 4 of [20].

In this method one has to fix $x_i^1$ and $x_i^2$ for all $i \in Y$. Since $\epsilon$ is a minimal volume for a parallelepiped spanned by $x_b - x_a, x_c - x_a, x_d - x_a$ for each ordered base $(a, b, c, d)$, the points $(x_a^1, x_a^2)$, $(x_b^1, x_b^2)$, $(x_c^1, x_c^2)$, $(x_d^1, x_d^2)$ cannot be on the same
straight line. We place all atoms of a molecule in a sequence and choose \( x_i^1 = \cos(2\pi i/n) \), \( x_i^2 = \sin(2\pi i/n) \) for all \( i \in V \) and \( \epsilon = (\sin(2\pi/n))^3 \), where \( n \) is a number of atoms.

In practical implementation of this algorithm of realization of a molecular partial chirotope, one has to set a partial chirotope of a given molecule. For example, for \( C^\alpha \) atom of amino acid residue it is necessary to set 3 ordered bases. Fixing only 2 of them jams vibrant iterative centering algorithm (the modification of iterative centering which will be described in Section 8) and fixing 4 of them is too restrictive for the choice of \( x_i^1 \) and \( x_i^2 \). The fourth ordered base will be recovered by means of distance constraints. Similarly, for \( C^\alpha \) atoms of one spire of \( \alpha \)-helix, in which participate 5 residues, it is necessary to set 3 ordered bases. This partial chirotope will be used also for chirality checking \( \text{CheckChirality}(u) \).

Consider an example of poly-L-threonine Thr\(_{180}\). Each Thr residue contains two chiral centers. For \( C^\beta \) atom of Thr residue it is necessary to set 3 ordered bases. Arrange 14 atoms of each Thr residue in a following order H-N-H-C\(^\alpha\)-C\(^\beta\)-H-O\(^\gamma\)-H-C\(^\gamma\)-H-H-H-C-O (or in the notations of Protein Data Bank H-N-H-CA-CB-H-OG1-H-CG2-H-H-C-O). The proposed algorithm successfully finds a realization of a corresponding partial chirotope. Let us add to this chirotope also the constraints on \( C^\alpha \) atoms which appear assuming Thr\(_{180}\) is twisted in 50 spires of right \( \alpha \)-helix. The algorithm successfully finds a realization in this case.

8 Metropolis Monte Carlo in the restricted sample space

If a given partial chirotope is realized, one has to transform this realization, keeping correct chiralities, in order to achieve \( \mathcal{D}(S) \) and then to start the Metropolis MC simulation in the restricted sample space. Let \( \text{CheckChirality}(u) \) be a function which checks whether quadruples of vertices which contain a vertex \( u \) satisfy a given
partial chirotepe. Numerical tests show that reiteration of the iterative centering algorithm with chirality checking can become jammed if the initial sample is far from $D(S)$. (For example, consider the weighted graph with four vertices and four edges on a plane: let the starting configuration be $A = (0, 0), B = (4, 3), C = (4, -3), D = (0, 5)$, the weights of $(A, B)$ and $(A, C)$ be 5, the weight of $(B, C)$ be 6, the weight of $(A, D)$ be 0.01, $B, C, D$ be counter-clockwise and $S(u) = 0.001$ for all vertices.) For overcoming this difficulty one can use the following modification of the iterative centering algorithm:

$$Vib\text{rant\text{ence}}(u)$$

1. $a \leftarrow A[u]$
2. $z \leftarrow Center(u)$
3. $r \leftarrow \|a - z\|$
4. if $r > C \cdot S[u]$
   5. then $A[u] \leftarrow a + C \cdot S[u] \cdot ((z - a)/r + c \cdot RandomVector())$
   6. else if $r > S[u]$
      7. then $A[u] \leftarrow a + S[u] \cdot ((z - a)/r + c \cdot RandomVector())$
      8. else $A[u] \leftarrow z + S[u] \cdot c \cdot RandomVector()$
9. if not $CheckChirality(u)$
10. then $A[u] \leftarrow a$

$RandomVector()$ denotes a function, which returns a uniformly distributed vector in a sphere of radius 1 with the center at the origin. A coefficient $c > 1$ is introduced for ergodicity. A coefficient $C > 1$ is introduced for speeding-up. There is no guarantee that $D(S)$ will be achieved, but the examples of this section show that the method works.

The vibrant iterative centering algorithm can be useful if the method described in Section 7 fails. Split some vertex from $Y$ into several vertices and spread the
inequalities of the form $\det(x_b - x_a, x_c - x_a, x_d - x_a) \geq \epsilon$ in which the coordinates of the initial vertex participate over these new vertices. In the weighted graph put the desired distances between the new vertices be 0. Do this for several vertices from $Y$. Apply the described linear programming method and the vibrant iterative centering to bring nearer the vertices obtained from the same vertex.

Introduce $\text{CheckDistance}$ function:

$$\text{CheckDistance}(u)$$

1. $x \leftarrow \text{head(Adj}[u]\text{)}$
2. while $x \neq \text{NIL}$
3. do $v \leftarrow \text{vertex}[x]$
4. if $\|A[v] - \text{Center}(v)\| < S[v]$ or $S[v] = 0$
5. then $x \leftarrow \text{next}[x]$
6. else return FALSE
7. return TRUE

Let us sum up the proposed methods in the following computing scheme:

$$\text{TrialMove}(u)$$

1. $a \leftarrow A[u]$
2. $A[u] \leftarrow a + S[u] \cdot \text{RandomVector}()$
3. if $\|A[u] - \text{Center}(u)\| < S[u]$ and $\text{CheckDistance}(u)$ and $\text{CheckChirality}(u)$
4. then $E \leftarrow \text{potential}(u)$
5. $z \leftarrow A[u]$
6. $A[u] \leftarrow a$
7. $e \leftarrow \text{potential}(u)$
8. if $E < e$ or $\text{Random}() < \exp((e - E)/(kT))$
9. then $A[u] \leftarrow z$
10. else $A[u] \leftarrow a$
\begin{verbatim}

z ← Center(u)

r ← ||a − z||

if r > S[u] or not CheckDistance(u)
    then if r > C · S[u]
        then A[u] ← a + C · S[u] · ((z − a)/r + c · RandomVector())
        else if r > S[u]
            then A[u] ← a + S[u] · ((z − a)/r + c · RandomVector())
            else A[u] ← z + S[u] · c · RandomVector()
    if not CheckChirality(u)
        then A[u] ← a

Random() generates a uniformly distributed in [0, 1] random number \[27\].

Now we apply the proposed methods in their natural succession: firstly a realization of partial chirotope, then vibrant iterative centering and then the Metropolis MC in the restricted sample space. If a conformation which satisfies chirality constraints is not given, then one can use the method of Section \[7\] to build such conformation. It is useful to rescale this conformation to its natural scale and proportions. Then one can start vibrant iterative centering with large \(S[u]\) to break frozen parts of the initial conformation and gradually decrease \(S[u]\) to required values. Then it is possible to start \texttt{TrialMove} over all atoms, which drives a molecule to \(D(S)\) and then becomes to be the Metropolis MC simulation in \(D(S)\). Similar to the original Metropolis MC \[28\], only coordinates of one atom are changed near its current position in a trial move. It makes the all-atom (including hydrogen) Metropolis MC possible also in the case of dense atom packing. Also \texttt{TrialMove} allows flexible manipulations with molecule by adding or removing weighted edges of the weighted graph and subsequent equilibration.

Consider an example of poly-L-alanine Ala_{36}, which is twisted in 10 spires of right \(\alpha\)-helix. We add to the weighted graph, which is derived from the primary
\end{verbatim}
structure of the molecule, distances of hydrogen bonds $O(i) - H(i+4)$, $O(i) - N(i+4)$ and distances $C_\alpha(i) - C_\alpha(i+2)$, which are well defined in $\alpha$-helix (the parentheses contain numbers of residues). Then we apply the simplex procedure, vibrant iterative centering algorithm and Metropolis MC simulation in the restricted sample space using Amber force field as described in the previous sections and receive the expected structure.

9 Molecular MC simulation without detailed balance using the quantum-classical isomorphism

In order to proceed to non-equilibrium molecular simulations we add pairs of particles similar to that described in the example of Section 3 to the considered molecule. These pairs of particles are used as artificial devices and do not represent physical particles. In this section we shall call these artificial added particles by beads for convenience. Also we add one Hooke term per bead to the molecule potential so that it connects a bead to some atom of a molecule by a spring with spring constant $h_a$ and zero length when the spring is relaxed. Suppose, that a sample which satisfies a given partial chirotope and distance constraints of such equipped molecule is built and equilibrated by methods described in previous sections. Subsequently we produce $K$ copies of this system which are connected by springs as described in the discussion of the quantum-classical isomorphism in Section 11.

In this loaded case we cannot use two Levy constructions for an added pair of beads as described in Section 3, but in order to approach to a process whose jumps obey the property of the balance of relative entropy let $K = 2j$ and choose the $l$-th added pair of beads with probability $p_l$, then uniformly choose two copies $n_1^i$ and $n_2^i = n_1^i + j$, fix the $n_1^i$-th copy of one bead from the $l$-th added pair and the
Consider the example of the linear polymer molecule which contains \( N = 16 \) identical atoms with some Lennard-Jones constants and with neighbor atoms connected by springs. We add one aforementioned pair of beads to each pair of neighbor atoms. We constrain the sequence of the second beads of the added pairs to have chiralities of right helix and produce two copies of this system which are connected by springs as described in Section 8. Then we start the simulation and observe that the polymer moves ahead. If one fixes the last atom in the space, then the polymer twists around the fixed atom like boa. The twisting polymer squeezes itself out. This observation hints on the possibility to use such method in molecular MC.
Appendix

The following notations are used in Table 1 and Table 2 (see Section 4 for details).

- $K$ the number of copies in the quantum-classical isomorphism,
- $j$ the superscript parameter of $\{N^j_t\}$ or $\{W^j_t\}$,
- $\alpha$ the probability parameter of $\{N^j_t\}$ or $\{W^j_t\}$,
- $J$ the number of forward and backward jumps,
- $F$ the number of forward jumps $i \leq J$ for which $\|a_{n_1}^i - b_{n_1}^i\| - \|a_{n_2}^i - b_{n_2}^i\|$ and $\|a_{n_1}^{i+1} - b_{n_1}^{i+1}\| - \|a_{n_2}^{i+1} - b_{n_2}^{i+1}\|$ have different signs,
- $R$ the number of backward jumps $i \leq J$ for which $\|a_{n_1}^i - b_{n_1}^i\| - \|a_{n_2}^i - b_{n_2}^i\|$ and $\|a_{n_1}^{i+1} - b_{n_1}^{i+1}\| - \|a_{n_2}^{i+1} - b_{n_2}^{i+1}\|$ have different signs,
- $A$ the average of coordinates $A = \frac{1}{K} \sum_{n=1}^{K} a_{n}^{J+1}$ after the last jump,
- $B$ the average $B = \frac{1}{K} \sum_{n=1}^{K} (b_{n}^{J+1} - \delta)$, where the first sample for the processes is $((0, \ldots, 0), (\delta, \ldots, \delta))$,
- $C$ the average number $C = \frac{1}{K} \sum_{n=1}^{K} C_n$, where $C_n$ is the number of $i \leq J$ such that $\|a_{n}^i - b_{n}^i\| - \|a_{n'}^i - b_{n'}^i\|$ and $\|a_{n}^{i+1} - b_{n}^{i+1}\| - \|a_{n'}^{i+1} - b_{n'}^{i+1}\|$ have different signs, where $n' \equiv n + j \pmod{K}$,

In the case of $\{N^j_t\}$ we take $J/C = 2$. The lengths in these tables are in units $\frac{\hbar}{\sqrt{mkT}}$. 

32
Table 1: Numerical results for $\left\{N_t^j\right\}$

| K | j  | $\alpha$ | $J$ | $F$ | $R$ | $A$  | $B$  | $\frac{(A+B)}{F}$ |
|---|----|-------|-----|-----|-----|-----|-----|------------------|
| 8 | 2  | 1.0000| 5002391 | 0   | 1.2212e+006 | 1.2242e+006 | 9.778e-001 |
| 8 | 2  | 0.6667| 3336249 | 1668173 | 4.0719e+005 | 4.0778e+005 | 9.773e-001 |
| 8 | 2  | 0.5833| 2919143 | 2081936 | 2.0472e+005 | 2.0419e+005 | 9.768e-001 |
| 8 | 2  | 0.5417| 5415950 | 4583516 | 2.0225e+005 | 2.0394e+005 | 9.758e-001 |
| 8 | 2  | 0.5208| 5205748 | 4792723 | 1.0111e+005 | 9.7748e+004 | 9.629e-001 |
| 16| 1  | 0.6667| 3331214 | 1667291 | 2.2680e+005 | 2.2837e+005 | 9.471e-001 |
| 16| 2  | 0.6667| 3333718 | 1666593 | 3.1050e+005 | 3.1231e+005 | 7.470e-001 |
| 16| 4  | 0.6667| 3332375 | 1668024 | 4.0726e+005 | 4.0476e+005 | 9.763e-001 |
| 16| 8  | 0.6667| 3332983 | 1667959 | 4.7057e+005 | 4.6881e+005 | 1.129e+000 |
| 32| 1  | 0.6667| 3333992 | 1665310 | 1.6566e+005 | 1.6342e+005 | 3.946e-001 |
| 32| 2  | 0.6667| 3334183 | 1666927 | 2.2823e+005 | 2.2691e+005 | 5.461e-001 |
| 32| 4  | 0.6667| 3335290 | 1664622 | 3.1246e+005 | 3.1090e+005 | 7.460e-001 |
| 32| 8  | 0.6667| 3334115 | 1665497 | 4.0766e+005 | 4.0893e+005 | 9.788e-001 |
| 64| 2  | 0.6667| 3333389 | 1665903 | 1.6270e+005 | 1.6609e+005 | 9.344e-001 |
| 64| 8  | 0.6667| 3334884 | 1667409 | 3.1174e+005 | 3.1077e+005 | 7.465e-001 |
| 64| 16 | 0.6667| 3333361 | 1665149 | 4.0878e+005 | 4.0681e+005 | 9.783e-001 |
Table 2: Numerical results for $\{W^J_t\}$
References

[1] M.P. Allen, D.J. Tildesley, Computer simulation of liquids, Clarendon Press, Oxford, 1987.

[2] Amber home page, amber.scripps.edu.

[3] A. Björner, M. Las Vergnas, B. Sturmfels, N. White, G.M. Ziegler, Oriented matroids, Encyclopedia of Mathematics and its Applications, 46. Cambridge University Press, Cambridge, 1993.

[4] L.M. Blumenthal, Theory and applications of distance geometry, Oxford, at the Clarendon Press, 1953.

[5] J. Bokowski, B. Sturmfels, On the coordinatization of oriented matroids, Discrete Comput. Geom. 1 (1986) no. 4, 293-306.

[6] F. Bonetto, J.L. Lebowitz, L. Rey-Bellet, Fourier’s law: a challenge to theorists, Mathematical physics 2000, Imp. Coll. Press, London (2000) 128-150. arXiv:math-ph/0002052

[7] W. Braun, N. Go, Calculation of protein conformations by proton-proton distance constraints, J. Mol. Biol. 186 (1985) 611-626.

[8] T.H. Cormen, C.E. Leiserson, R.L. Rivest, Introduction to algorithms. The MIT Electrical Engineering and Computer Science Series. MIT Press, Cambridge, MA; McGraw-Hill Book Co., New York, 1990.

[9] G.M. Crippen, T.F. Havel, Distance geometry and molecular conformation. Chemometrics Series, 15. Research Studies Press, Ltd., Chichester; John Wiley & Sons, Inc., New York, 1988.

[10] L. Devroye, Nonuniform random variate generation, Springer-Verlag, New York, 1986. http://cg.scs.carleton.ca/~luc/rnbookindex.html

35
[11] Y. Duan and P. Kollman, Pathways to a protein folding intermediate observed in a 1-microsecond simulation in aqueous solution, *Science* 282 (1998) 740-743.

[12] R.P. Feynman, A.R. Hibbs, *Quantum mechanics and path integrals*, McGraw-Hill Book Company, New York, 1965.

[13] M.P. Frank, Requirements for practical reversible computing, Solid State Seminar, Notre Dame, April 19, 2005.
   www.eng.fsu.edu/~mpf/ND-Frank-ReqPracRevComp.ppt

[14] D. Frenkel, B. Smit, *Understanding molecular simulation: from algorithms to applications*, Academic Press, New York, 1996.

[15] P. Gaspard, Brownian motion, dynamical randomness and irreversibility, *New J. of Phys.* 7 (2005) 77.1-77.19 (electronic).

[16] I.S. Gradshteyn, I.M. Ryzhik, *Tables of integrals, sums, series and products*, Fizmatgiz, Moscow, 1963.

[17] R.M. Gray, *Entropy and information theory*, Springer Verlag, New York, 1990.

[18] K. Huang, *Statistical mechanics*, 2ed., J. Wiley & Sons, New York, 1987.

[19] *Encyclopedic Dictionary of Mathematics*, Second Edition by the Mathematical Society of Japan, edited by Kiyosi Ito, The MIT Press, Cambridge, Massachusetts, and London, England, 1993.

[20] M.W. Jeter, *Mathematical programming. An introduction to optimization. Monographs and Textbooks in Pure and Applied Mathematics, 102*. Marcel Dekker, Inc., New York, 1986.

[21] J. Kurchan, Fluctuation theorem for stochastic dynamics, *J. Phys. A* 31 (1998) 3719-3729. arXiv:cond-mat/9709304
[22] M. Laurent, Polynomial instances of the positive semidefinite and Euclidean distance matrix completion problems, \textit{SIAM J. Matrix Anal. Appl.} 22 (2000) no.3, 874-894 (electronic).

[23] J.L. Lebowitz, H. Spohn, A Gallavotti-Cohen-type symmetry in the large deviation functional for stochastic dynamics, \textit{J. Stat. Phys.} 95 (1999) no. 1-2, 333-365. \texttt{arXiv:cond-mat/9811220}

[24] P. Lévy, Sur certains processus stochastiques homogénes. \textit{Compositio Math.}, 7 (1939) 283.

[25] A.N. Matveev, \textit{Optics}, Mir, Moscow 1988.

[26] V.I. Manousiouthakis, M.W. Deem, Strict detailed balance is unnecessary in Monte Carlo simulation, \textit{J. of Chemical Physics}, 110 (1999) no. 6, 2753-2756.

[27] M. Matsumoto, T. Nishimura, Mersenne Twister: A 623-dimensionally equidistributed uniform pseudo-random number generator, \textit{ACM Transactions on Modeling and Computer Simulation}, 8 (1998) no. 1, 3-30. www.math.sci.hiroshima-u.ac.jp/ m-mat/MT/emt.html

[28] N. Metropolis, A.W. Rosenbluth, M.N. Rosenbluth, A.H. Teller, E. Teller, Equation of state calculations by fast computing machines, \textit{J. of Chemical Physics}, 21 (1953) no. 6, 1087-1092.

[29] J. More, Z. Wu, epsilon-optimal solutions to distance geometry problems via global continuation. Global minimization of nonconvex energy functions: molecular conformation and protein folding (New Brunswick, NJ, 1995), \textit{DIMACS Ser. Discrete Math. Theoret. Comput. Sci.}, 23, Amer. Math. Soc., Providence, RI (1996) 151-168.

[30] O. Narayan, A.P. Young, Convergence of Monte Carlo simulations to equilibrium, \textit{Phys. Rev. E}, 64 (2001) 021104-1 – 021104-4.
[31] NMRchitect, Accelrys Inc. 2001

http://nmr.ulaval.ca/labo/insight/doc/life/insight2000.1/nmr/nmr980TOC.doc.html

[32] F. Oberhettinger, Fourier Transforms of Distributions and Their Inverses. A collection of tables, Academic Press, New York and London, 1973.

[33] Y. Okamoto, Metropolis algorithms in generalized ensemble, arXiv:cond-mat/0308119, 2003.

[34] J.C. Phillips, R. Braun, W. Wang, J. Gumbart, E. Tajkhorshid, E. Villa, C. Chipot, R.D. Skeel, L. Kale, K. Schulten, Scalable molecular dynamics with NAMD, J. Comput. Chem., 26 (2005) 1781-1802. www.ks.uiuc.edu/Publications/Papers/PDF/PHIL2005/PHIL2005.pdf

[35] J.W. Pitera, W. Swope, Understanding folding and design: replica-exchange simulations of ”Trp-cage” miniproteins, Proc. Natl. Acad. Sci. USA, 100 (2005) no. 13, 7587-7592.

[36] J.P. Ryckaert, G. Ciccotti, H.J.C. Berendsen, Numerical integration of the cartesian equations of motion of a system with constraints; molecular dynamics of n-alkanes, J. Comput. Phys., 23 (1977) 327-341.

[37] J.B. Saxe, Embeddability of weighted graphs in k-space is strongly NP-hard, in: Proc. 17th Allerton Conference in Communications, Control and Computing (1979) 480-489.

[38] J. Shimada, E.L. Kussel, E.I. Shakhnovich, The folding thermodynamics and kinetics of crambin using an all-atom Monte Carlo simulation, J. Mol. Biol., 308 (2001) 79-95.
[39] J. Skolnick, A. Kolinski, Monte Carlo approaches to protein folding problem, in: *Advances in Chemical Physics*, v. 105, *Monte Carlo Methods in Chemical Physics*, John Wiley & Sons, 1999.

[40] A.D. Sokal, Monte Carlo methods in statistical mechanics: foundations and new algorithms, *Lectures at the Cargese summer school on “Functional integration: basics and applications”* (Cargese, 1996), NATO Adv. Sci. Inst. Ser. B Phys., 361, Plenum, New York, (1997) 131-192. www.math.nyu.edu/faculty/ goodman/teaching/Monte_Carlo/Sokal.ps

[41] I.T. Todorov, W. Smith, The DL_POLY_3 user manual, CCLRC Daresbury Laboratory, Daresbury, Warrington, Cheshire, UK, 2006. www.cse.scitech.ac.uk/ccg/software/ DL_POLY/MANUALS/USRMAN3.07.pdf

[42] F. Tschirschnitz, Testing extendability for partial chirotopes is NP-complete. *Proceedings of the 13th Canadian Conference on Computational Geometry*, U. of Waterloo, Ontario, Canada, (2001) 165-168. www.cccg.ca/proceedings/2001/

[43] M. Vendruscolo, E.Kussel, E. Domany, Recovery of protein structure from contact maps, *Folding and Design*, 2 (1997) 295-306.

[44] G.M. Ziegler, Oriented matroids today, *Electron. J. of Combin.* 3 (1996), no.1, Dynamic Survey, 39pp.(electronic).