Effect of excluded volume on 2D discrete stochastic chemical kinetics

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Abstract: The Stochastic Simulation Algorithm (SSA) is widely used in the discrete stochastic simulation of chemical kinetics. The propensity functions which play a central role in this algorithm have been derived under the point-molecule assumption, i.e., that the total volume of the molecules is negligible compared to the volume of the container. It has been shown analytically that for a one dimensional system and the A+A reaction, when the point molecule assumption is relaxed, the propensity function need only be adjusted by replacing the total volume of the system with the free volume of the system.

In this paper we investigate via numerical simulations the impact of relaxing the point-molecule assumption in two dimensions. We find that the distribution of times to the first collision is close to exponential in most cases, so that the formalism of the propensity function is still applicable. In addition, we find that the area excluded by the molecules in two dimensions is usually higher than their close-packed area, requiring a larger correction to the propensity function than just the replacement of the total volume by the free volume.

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1. INTRODUCTION

The Stochastic Simulation Algorithm (SSA) [1] is the workhorse algorithm for discrete stochastic simulation of networks of coupled chemical reactions. The physical system, in this case, is a collection of molecules of various chemical species that move around inside a fixed volume, and are subject to a set of chemical reactions in which the molecules may be reactants or products or both. The chemical reactions are all assumed to be “elementary" in the sense that they occur essentially instantaneously. Elementary reactions will invariably be either unimolecular or bimolecular; all other types of reactions (trimolecular, reversible, etc.) will consist of a series of two or more elementary reactions. If the system is well-stirred, we can define its state simply by giving the vector $\mathbf{x}$ of the molecular populations of the various chemical species. In that circumstance, it is usually possible to describe the dynamics of each reaction channel $R_j$ by a "propensity function" $a_j(\mathbf{x})$, defined so that if the system is in state $\mathbf{x}$, then $a_j(\mathbf{x})dt$ gives the probability that the reaction will occur somewhere inside the system in the next infinitesimal time interval $dt$. The magnitude of $a_j(\mathbf{x})$ thus measures the "propensity" of reaction $R_j$ to occur in the immediate future.

The propensity function is very close to, and sometimes numerically equal to, what in deterministic chemical kinetics is called the "reaction rate". But the propensity function does not make the assumption that reactions occur continuously and deterministically,
and its product with $dt$ is mathematically treated as a probability. The outcome of such a set of assumptions is the chemical master equation (CME) and the stochastic simulation algorithm (SSA), as discussed in numerous articles over the past three decades [1]. In the thermodynamic limit (infinite populations and infinite system volume with finite concentrations), the CME and SSA almost always reduce to the ordinary differential equations of deterministic chemical kinetics.

The SSA generates times $\tau$ between successive reactions as samples of an exponential distribution whose mean is equal to the inverse of the sum of the propensity functions. The most commonly used propensity functions are of a mass action form, according to which the rate of a reaction is proportional to the combinatorial product of the reactants’ populations.

Mass action propensity functions for elementary reactions have been rigorously derived in a well-stirred, dilute hard sphere setting [2]. In this setting molecules are represented by hard spheres moving ballistically in a vacuum. We refer to them as point molecules, because, although they must have non-zero diameter $l$ in order to collide, the volume of all the molecules combined is negligible compared to the volume of their container. If the point molecule assumption is relaxed, to what extent does the volume occupied by the reactant molecules themselves affect the rates of the reactions in which they participate?

We will be studying the effect of reactant-excluded volume, in a simple but computationally tractable physical model. Specifically, we will attempt to answer the
following two questions. First, is the time between successive reactions in a well-stirred, non-point molecule system exponentially distributed, as it must be for the stochastic process theory which underlies the SSA to hold? Second, if the reaction times are exponentially distributed, what is the mathematical form of the propensity functions in this setting?

Since bimolecular reactions are always initiated by a collision, the probability of a reaction between two molecules can be broken down into a) the probability that the two molecules will collide, times b) the probability that they will react given that they have collided. Throughout this work we make the simplifying assumption that (b) is unity, and thus use the terms collision and reaction probability (and inter-collision and inter-reaction time) interchangeably.

We have previously shown how, for a one dimensional system, the mass action propensity functions need to be modified when the volume of the reactant molecules is comparable to the total system volume [3]. We analytically derived the following exact formula for the reaction probability, in the next infinitesimal time $dt$, of the reaction $A + A \rightarrow \text{products}$ in a one-dimensional system of $N$ non-overlapping hard rods of length $l$ moving ballistically in a volume of length $L$:

$$p_{\text{col}}(dt) = \frac{N(N - 1)s_{\text{rel}}}{2(L - NI)} dt .$$  

(In the limit of $l \rightarrow 0$ this is equal to the usual dilute gas reaction rate law.) The propensity function for the reaction is, by definition, this probability divided by $dt$. In Eq. (1), $s_{\text{rel}}$ is the mean relative speed of two randomly chosen rods. The correctness of
this formula was then confirmed through an extensive series of exact hard rod molecular
dynamics simulations.

An analogous treatment of the two-dimensional hard disc system has proved to be
challenging. The difficulty arises when trying to find an analytical intermolecular
distance distribution function for non-overlapping, non-zero sized hard disks in a finite
area. The one dimensional case, given in [3] is essentially a consequence of the Tonks
result [4]. But, to the best of our knowledge, a two or three-dimensional exact version has
not been reported in the literature, and we have not been able to derive it ourselves.

Thus, in this paper we use the hard spheres molecular dynamics simulation methodology
to \textit{computationally} investigate the effect of molecule size on the propensity for the
\( A + A \rightarrow \text{products} \) reaction in the two-dimensional version of the system. We consider a
system of \( N \) hard disks, each of diameter \( l \), initially distributed uniformly randomly
with no overlap inside a circular container with hard reflective walls and diameter \( L \). The
choice of hard instead of periodic boundaries was made after careful consideration. We
believe that hard boundaries bring our simple system closer to being “realistic”. Periodic
boundaries would introduce the unphysical “appearance” of molecules from nowhere, as
they cross the boundary. Also, for molecules that have nonzero diameter, periodic
boundaries make choices regarding initial random placement and inter-molecular
collision detection awkward, if not arbitrary.
The molecules move ballistically, and their initial velocities are drawn from a Maxwell-Boltzmann distribution. These initial conditions represent a well-stirred system in thermal equilibrium. For this system, we collect statistics for the time $\tau$ from the initialization of the system until the first inter-molecular collision. We will not be concerned with the evolution of the system beyond the first collision, because our goal here is simply to study the form of the propensity functions when the well-stirred condition, which is assumed by the SSA, holds before each reaction. The question of under what conditions such a system will return to a well-stirred state is both interesting and important, but we do not address that question in this paper. We do, however, briefly consider the effect of container shape on our results.

We find that the distribution of inter-collision times $\tau$ in this system is approximately exponential, but with noticeable deviations in certain circumstances. We study how the $\tau$ distribution varies with the parameters $l$ and $L$, which, for a fixed $N$, determine the area density of the system (defined as the ratio of the area of the molecule disks to the total area of the system).

For small numbers of molecules, it appears that three types of $\tau$ distribution are present: at intermediate values of the area density, the distribution is indistinguishable from an exponential; as the system tends to the point molecule limit (low area density), long inter-molecular collision times are overrepresented; as the area density of the system becomes high, short inter-molecular collision times are overrepresented.
It is known that the choice of container shape affects the degree of ergodicity of the molecules’ trajectories, with some container shapes encouraging trajectories that sample only small parts of the container’s area. In the low population and small molecule size limit, we find that the small number of molecules, combined with a choice of non-ergodic container shape (e.g. circular, as opposed to “stadium”), gives rise to over-represented long times, while the $\tau$ distribution for short times is just as predicted theoretically. Either increasing the number of molecules, or improving the shape of the boundary, ameliorates this effect.

As the area density of the system becomes high (i.e. for large $l/L$), and for low population, we find that the excluded area inferred from the simulation measurements is larger than what one might expect from taking into account the area of the molecule disks, or their close-packed area, or even several less dense packings [5]. However, as the number of molecules is increased, the excluded area approaches the close-packed area, as one might have expected.

These results suggest that excluded area in two and three dimensional, finite, dense systems has a somewhat predictable impact for systems with a large number of molecules, but may have greater impact than one might have initially supposed for systems with low population.

In section 2 we present the physical system under consideration and the computational algorithms used to simulate its kinetics. In section 3 we give a brief derivation of the
probability of collision from first principles. In section 4 we present the results of our simulations. Section 5 summarizes and attempts to explain our findings.

2. HARD SPHERE MOLECULAR DYNAMICS

A. The Hard Sphere Molecular Dynamics algorithm

The hard sphere molecular dynamics simulation algorithm is a simple billiard balls simulator. Given randomly uniform initial positions and random Maxwellian velocities for the molecules, it returns the time to the first inter-molecular collision.

The algorithm, as used for the two-dimensional problem, has the following steps:

1. Initialize \( N \) molecules, each a disk of diameter \( l \), with:
   a. uniform random non-overlapping positions in a finite container of area \( A \)
      (see placement algorithms in subsections B and C);
   b. velocities distributed according to the Maxwell-Boltzmann distribution

2. For each molecule, compute the next putative collision time with the boundary of the system (ignoring all the other molecules in the system).

3. For each pair of molecules, compute the next putative inter-molecular collision time, if it exists.

4. Choose the smallest of all molecule-boundary and inter-molecular collision times, and advance the time by that amount.

5. If the collision was:
   a. inter-molecular, then report the time and exit;
b. between a molecule and the boundary, then reflect the colliding molecule according to a specular reflection formula; advance the positions of the remaining molecules, and go back to step 2.

The velocities of the molecules are Maxwell-Boltzmann distributed, meaning that each Cartesian component of the velocity vector is a statistically independent normal random variable with mean 0 and temperature-determined variance $\sigma^2$.

Statistics for the distribution of times $\tau$ to the first collision are obtained by running an ensemble of 100,000 realizations of the hard spheres molecular dynamics algorithm (for a given $N$, $l$, and $L$), each with different random seeds.

**B. Generating exact initial positions**

For the one-dimensional problem it was possible to derive a rejection-free Monte Carlo algorithm for generating samples of the molecules' initial positions. An analogous procedure for two dimensions has proven elusive (this problem is equivalent to finding the analytical formula for the intermolecular distance distribution function), so a rejection based Monte Carlo algorithm was used to generate uniform random non-overlapping positions for the molecules in two dimensions.

The rejection-based initial placement algorithm has the following steps:

For molecule index $i = 1, \ldots, N$:
1. Generate putative coordinates \((x_i, y_i)\) for the center of molecule \(i\) uniformly and randomly inside the container.

2. Check whether the proposed placement will overlap any of the \((i - 1)\) previously placed molecules
   a. If an overlap is discovered, discard the entire set of placed molecules (indices 1, \ldots, \(i\)). Reset the index to \(i = 1\) and restart the procedure.
   b. If no overlap is discovered, accept the placement, increment the index and go to step 1.

Step (2a) is the only non-obvious step of the placement algorithm: we discard the entire set of already placed molecules, as opposed to only the very last one, which produced the overlap. The latter procedure will result in a biased distribution, as can be demonstrated both analytically and by numerical simulation in a one-dimensional setting.

The computational cost of this rejection-based method increases with the total number of molecules, and with the area density of the system. The simulations we were able to perform using this placement method reached up to area densities of 40% for small values of \(N\) (e.g. \(N=6\)).

C. Generating approximate initial positions

One approximate alternative to generating the initial positions of the molecules by the rejection-based Monte Carlo method is to use a \textit{pre-stirring} procedure. In this scheme we initialize the positions of the molecules on a regular grid and then allow the molecules to
bounce around until their positions are randomized. The success of such an initialization depends on choosing a good stopping condition. This can be: a) a time by which an ensemble of positions is guaranteed to have become well-stirred, b) a target value for a function (e.g. the radial distribution function), which when reached would denote a well-stirred state, or c) noticing that a function (again, possibly the radial distribution function) appears to have converged, without explicitly having a target value for it. We were unable to locate either (a) or (b) in the literature, and our experience with checking the radial distribution function for convergence suggested that it was too noisy for systems with small numbers of molecules.

There is a subtle aspect to choosing the stopping criterion when the system is simulated not by traditional Molecular Dynamics (i.e. integration of the laws of motion), but by our exact hard sphere algorithm, which steps from collision to collision. If we stop pre-stirring the system *immediately* after an intermolecular collision has occurred, the two molecules which have just collided will be touching. Thus, choosing a stopping criterion that is based on the idea that an *exact* number of collisions must occur before stopping will yield ensembles of initial positions which systematically contain two molecules touching. One must remember to remove such a bias by evolving the system for some time past the last collision, or avoid introducing such a bias in the first place, by choosing a stopping condition expressed as a duration of time rather than number of collisions. We do the latter.
In our experiments exploring different amounts of pre-stirring we found that
unexpectedly long amounts of pre-stirring time were necessary for other indicators, e.g.
the mean of $\tau$, which is the focus of this paper, to reach the values obtained by the
rejection-based method. For a given system (i.e. given $N, l, L$) we quantify the duration of
pre-stirring as $FN\bar{\mu}_r$ units of time, where $F$ is a scaling factor, $N$ is the number of
molecules, and $\bar{\mu}_r$ is the expected time to the first collision for this system, under the
assumption that $V_e = V_d = Na$ (see section 3). Figure 1 shows, for a system with $N=9,
L=10, l=2$, how the mean time to the first collision computed by simulations initialized
with pre-stirring (circles) approaches that computed by a simulation initialized by
rejection-based Monte Carlo (solid line with dashed confidence interval), with increasing
$F$.

For a factor $F=300$, and the system of Figure 1 ($N=9$), we see on average 4113
intermolecular collisions, i.e. each molecule experiences on average 457 collisions with
another molecule. We also see on average 2401 collisions with the boundary, i.e. on
average 267 collisions with the boundary per molecule. So $F$ is a conservative estimate of
the number of intermolecular collisions each molecule experiences during the pre-stirring
simulation.

While the pre-stirring method of obtaining initial positions makes it possible to work with
dense, high-population systems which we would otherwise not have been able to
examine, it is nevertheless very time consuming. As can be seen from Figure 1, $F=300$ is
suboptimal in terms of achieving good stirring (if the mean of the $\tau$-distribution is used
as a convergence criterion). However it would take 10 times as long to simulate with 
$F=3000$, in order to achieve the dubious improvement of having the 95% confidence 
interval of the pre-stirring method overlap that of the rejection-based Monte Carlo. 
Simulating ensembles of size 100,000 with a stirring factor of $F=300$ already takes days 
on a workstation, so the results we show in this paper are based on simulations with 
$F=300$, rather than a higher value.

Due to the lack of a rigor of our pre-stirring method, we do not consider it to be on equal 
footing with the rejection-based Monte Carlo. Nearly all the results in this paper were 
obtained using simulations initialized by rejection-based Monte Carlo. The single 
exception is Figure 7, which would have been impossible to obtain by rejection-based 
Monte Carlo, and which we therefore consider *speculative*.

3. THEORY FOR THE TWO-DIMENSIONAL CASE

Here we derive an expression for the probability $p_{\text{col}}(dt)$ of an inter-molecular collision 
 occurring in the next infinitesimal time interval $dt$. This probability is given by the 
 product of: (the number of ways one can choose a random pair of molecules) times (the 
 probability that a randomly chosen pair of molecules will collide in the next $dt$). Because 
of the randomly uniform spatial distribution, the second factor can be further decomposed 
into the ratio: (the area one molecule will sweep out relative to the other molecule in the 
next $dt$) over (the total area inside the container accessible to the other molecule).
The initial velocities of the molecules are assumed to follow the equilibrium Maxwell-Boltzmann distribution, i.e. their Cartesian components are normal random variables with means 0 and variances \( \sigma^2 = k_B T / m \), where \( T \) is the absolute temperature of the system, \( m \) is the mass of the molecules and \( k_B \) is Boltzmann’s constant. The mean relative speed of two randomly chosen molecules in such a distribution can be shown to be

\[
s_{\text{rel}} = \langle |v_{\text{rel}}| \rangle = \sqrt{\pi} \sigma.
\]  

(2)

Suppose we randomly choose a pair of molecules. We can do this in \( \frac{1}{2}N(N-1) \) ways.

Now we change our frame of reference so that we are standing on one of the chosen molecules. Then the area swept out by the other molecule in the next infinitesimal time increment \( dt \) relative to the center of the one we are standing on is (see Fig. 2) \( 2ls_{\text{rel}}dt \).

To get the probability of our randomly chosen pair of molecules colliding in the next \( dt \), we must divide this area by the total area available to the molecules. If we assume that the molecules have no extent \( (l = 0) \), the area \( A \) available to the molecules is the total area of the system. If the shape of the container is circular, and the diameter is \( L \), the area is given by \( A_c = \frac{1}{4} \pi L^2 \). For a “stadium” container (formally known as a Bunimovich stadium [6]), in which semi-circles of diameter \( L \) are separated by a square of side \( L \), the area is \( A_s = \frac{1}{4} \pi L^2 + L^2 \).

If we relax the point molecule assumption (i.e. \( l > 0 \)), the area available to the molecules will be less than the total area \( A \) of the system by \textit{at least} the area excluded by the disks.
of the molecules themselves \( V_d = Na = \frac{1}{4} \pi l^2 \). The question of exactly how large is the excluded area has prompted this research. We will call the excluded area as estimated from the simulation data the \textit{effective excluded area} \( V_e \), and we will show in the results section that it is quite a bit larger than \( V_d \).

Finally, combining all of the above, we find that the probability of an inter-molecular collision in the next \( dt \) is given by:

\[
p_{\text{col}}(dt) = \frac{2l_{\text{rel}}}{2} \frac{2ls_{\text{rel}}}{A - V_e} dt
\]

with \( V_e = 0 \) at the limit \( l = 0 \).

If we assume that the same probability \( p_{\text{col}}(dt) \) holds for each successive infinitesimal time increment \( dt \), from the initialization of the system until the first inter-molecular collision occurs, then the times \( \tau \) will be samples of the exponential distribution whose mean is the inverse of the coefficient of \( dt \) in Eq. (3). If we further assume that every collision results in a reaction, that coefficient will be the propensity function of the Stochastic Simulation Algorithm and the master equation for that reaction [1].

4. SIMULATION RESULTS

A. Collision time distribution methodology
To fully characterize the distributions of times to the first collision, $\tau$, we asked the following questions: what is the empirical distribution of $\tau$ at different area densities, and what is the relationship between this empirical distribution and the analytical exponential in Equation (3) with the most conservative estimate of excluded volume ($V_e = V_d = Na$)?

Upon casual visual inspection, all the distributions certainly appear exponential. To quantitatively test for exponentiality, we used a common two-sample comparison test, the Kolmogorov-Smirnoff test [7]. To test a $\tau$ distribution (100,000 values) for exponentiality, we generated the same number of random samples from an exponential with the same mean as the $\tau$ distribution. We then used Matlab’s `kstest` routine at the default significance level $\alpha = 0.05$. The routine rejects the null hypothesis that the samples came from the same distribution (exponential) if the so-called $p$-value returned by the test is $< 0.05$; it fails to reject the null hypothesis that the samples came from the same distribution, if the $p$-value is $> 0.05$.

**B. Collision time distribution for $N=6$**

We began by considering the low molecule count case $N = 6$, with $\sigma = 1$ in a circular container of diameter $L$. Figure 3 shows the regions of $(L,l)$ phase space where the distribution of $\tau$ is or is not statistically indistinguishable from an exponential according to the K-S test. At intermediate values of area density, for ensembles denoted with ‘+’,
the distribution is indistinguishable from the exponential. At low and high area density values, for ensembles denoted with ‘o’, the distribution deviates from the exponential.

However, the p-value of the K-S test does not reveal how the empirical $\tau$ distribution differs from an exponential distribution. To gain some insight into this issue, we note that the standard deviation of an exponential distribution is equal to its mean. We therefore computed the mean $\mu_{\tau}$ and the standard deviation $\sigma_{\tau}$ of the empirical $\tau$ distribution, and then examined the quantity $I_{\tau} = (\sigma_{\tau}/\mu_{\tau}) - 1$. If $\tau$ were exponentially distributed, we would have $I_{\tau} = 0$. If $I_{\tau} < 0$ the empirical $\tau$ distribution would be more peaked around its mean than an exponential distribution would be, and if $I_{\tau} > 0$ the empirical $\tau$ distribution would be more spread out than an exponential distribution.

The grayscale portion of Figure 3 gives a plot of $I_{\tau}$, again for $N = 6$ and $\sigma = 1$, in the $(L,l)$-plane. The plot shows where the distribution of $\tau$ is more spread out or less spread out than an exponential. One possible interpretation of this plot is the following: a large portion of the distribution of the $\tau$ sample is exponential, but superimposed on that is a component that ruins the overall exponentiality. In areas with $I_{\tau} < 0$ the values in the added component are close to the mean, i.e. small. In areas with $I_{\tau} > 0$ the values in the added component are larger than the mean. The latter component, in fact, contains some very large outliers.
This can be seen by comparing the hypothesized analytical exponential, whose mean is
given by the inverse of the coefficient of \( dt \) in equation (3), to the histogram of the \( \tau \)
data. An instance of a system for which \( I_\tau > 0 \) is the “small” molecule case \( \sigma = 1 \),
\( N = 6 \), \( L = 35 \), \( l = 0.1 \). The mean for the data is \(~191\) and the standard deviation is \(~204\).

Figure 4 breaks down the pdf of the \( \tau \) distribution into three segments for clarity (note
the different scales on the vertical axes). For shorter times (top plot), the empirical \( \tau \)
distribution (solid line) follows our analytical prediction (dashed line) very well.
Approximately two standard deviations to the right of the mean (\(~600\), middle plot), the
data becomes heavier than that model prediction, and is better described by an
exponential with the empirical mean (dotted line). Finally, at long times (bottom plot),
the data is heavier than both exponentials. So it appears that, in the \( I_\tau > 0 \) regime, the
data follows the analytical exponential at shorter \( \tau \) values, but has heavier than
exponential tails for long \( \tau \) values.

To better understand this behavior, we looked at some of the realizations that contributed
the outlier \( \tau \) samples, i.e. very long times. The trajectories of the molecules in those
systems were notable for their non-ergodicity; more specifically, there would frequently
be one or more molecules that moved along the circle boundary (a “whispering gallery”
mode [8]), or that crossed very close to the center (and therefore bounced back and forth
along the diameter). These trajectories are non-ergodic in the sense that the molecules are
not sampling the entire container volume. This has the effect of reducing the number of
potential pairings of molecules, which is small to begin with, thereby reducing the
probability that \textit{some} pair will collide. In this way, the \textit{shape} of the container boundary
combined with the small number of molecules contributes to the increased number of long-time outliers in the \( \tau \) distribution.

One is also led to suspect the boundary’s role from the observation that the number of boundary collisions preceding each inter-molecular collision increases dramatically as one approaches the point molecule limit – something that does not happen in a one-dimensional system. To test the hypothesis that the boundary contributes to the over-represented long times, we tried several modifications to the hard circular boundary that we initially studied.

One class of modifications left the shape of the boundary intact, but changed how the molecules were reflected after they struck it. Since our hypothesis is that specular reflections from the circular boundary tend to orchestrate the molecules’ trajectories in such a way that they did not always sample the entire space, we modified the reflection formulas in several ways, in an attempt to increase the randomness in the trajectory of the molecules as they depart the boundary. First, we completely randomized the departing velocity of the molecule after a collision, while keeping the speed constant. Surprisingly, this had the effect of further lengthening the mean collision time. We next tried adding a small random angle to the departure angle after a reflection. This had the effect of very slightly shifting the mean collision time towards the model mean. Both of these were ways that intuitively seemed to us as though they would increase the ergodicity of the trajectories in the system; yet, they yielded very inconclusive results.
The other class of modification that we tried retained specular reflection but changed the shape of the boundary to one which is supposed to discourage non-ergodic trajectories. More specifically, we moved from a circular boundary to a “Bunimovich stadium” [6]. This is simply the interior of a boundary made by joining two semi-circles of diameter $L$ with a square of side $L$ in between. This boundary shape is supposed to create fewer non-ergodic trajectories than either a square or a circle boundary alone. Indeed, we observed that it affected the $\tau$ distribution by moving its mean slightly, but noticeably, closer to the analytically predicted mean, and also the standard deviation closer to the mean (as it should be for an exponential). For instance when comparing two 400K run ensembles with $\sigma=1$, $N=6$, $l=0.1$, one in a circular container of diameter $L=30$, $A=706.9$ and the other in a stadium with $L=19.9$, $A=707.0$, we found a mean $\tau$ of 140.9 for the circle and 138.9 for the Bunimovich stadium, along with a standard deviation of 149.5 for the circle and 145.9 for the stadium. The analytical mean and standard deviation of $\tau$ for a volume of this area are 132.9. We confirmed that the effect is general by noticing that the $p$-values for the K-S exponentiality test imply that the test is much closer to accepting the distributions as exponential for Bunimovich stadium volumes than for circular volumes of the same area.

It seems to us that whether a boundary’s shape and reflection characteristics contribute to non-ergodic trajectories is not a simple yes-or-no question, but rather one of degree. Some boundaries will cause molecules’ trajectories to sample the container’s area in a shorter amount of time than others. Our simulations would be mostly affected by the degree of ergodicity within a set finite amount of time (the expected time to a collision), not “eventually”. Thus, we suspect that there is no such thing as an “ideal” boundary that
would completely eliminate the effects of non-ergodic trajectories. If this is so, then it is not surprising that the Bunimovich stadium did not completely abolish the long-time tails; instead, it is satisfying that it produced a measurable change in the expected direction.

At the other extreme of the area density, we see a different picture. An example system for which \( I_\tau < 0 \) is given by the “large” molecule case \( \sigma = 1, N = 6, L = 10, l = 2.8 \). The mean for the data is \( \sim 0.1511 \) and the standard deviation is \( \sim 0.1460 \). Figure 5 gives a breakdown of the pdf of the \( \tau \) distribution for those parameters. The most noticeable feature of the pdf is the complete mismatch between the model exponential curve (dashed line) and the data (solid line). This is due to the fact that the model exponential (dashed line) is computed using the very conservative estimate that \( V_c = Na \). But we see that the exponential curve with the empirical mean (dotted curve) follows the data (solid line) rather well. The major deviation in that regard is that at about two standard deviations to the right of the mean (\( \sim 0.5 \)), the data slightly undershoots the dotted exponential curve, which has the effect of biasing the mass of the distribution closer to the mean.

\[ \text{C. Collision time distribution for large population} \]

We have shown that in the low molecule population and low area density case the small number of molecules conspires with the non-ergodic boundary to introduce long-time outliers in the \( \tau \)-distribution. Figure 6 shows that increasing the number of molecules
while maintaining the low area density abolishes this effect, restoring exponentiality to the distribution.

But is it also the case that the low population but high area density non-exponentiality, which we described in the previous section, can be abolished by increasing the number of molecules? A definitive answer to this question could be given if our exact simulation methodology were tractable on dense, high N systems. However, the rejection-based Monte Carlo initialization of the positions of the molecules takes prohibitively long to complete for such systems. A tentative answer, which is hopefully a hint in the right direction, can be obtained using the pre-stirring based molecule position initialization routine. Figure 7a shows that increasing the number of molecules while maintaining a high area density restores exponentiality to the τ -distribution. (We will discuss figures 7b and 7c in the next section.)

D. Excluded volume

Our initial goal in this effort was to investigate the effect of reactant-excluded volume on the kinetics of the $A + A \rightarrow \text{products}$ reaction in our simulation experiments. The most straightforward way to estimate the excluded volume felt by the molecules in these experiments is to proceed as follows: Assume the distribution of $\tau$ to be exponential; then estimate the propensity $P$ as the inverse of the mean $\mu_\tau$ of the empirical $\tau$ -distribution; finally, compute the effective excluded volume by solving the following equation for $V_e$: 
\[
\frac{1}{\mu_r} = P = \frac{N(N-1)}{2} \frac{2ls_{rel}}{A - V_e}
\]

(4)

The effective excluded volume computed this way can then be compared to several “theoretically plausible” excluded volume formulas. The simplest such formula takes into account only the area excluded by the disk molecules themselves: \( V_d = Na \).

Another possibility would be to consider volumes of the form \( V_i = Na/\phi_i \), where \( \phi_i \) is a packing fraction. Some packing fractions that have been theoretically studied by others are: \( \phi_{cp} = \pi/2\sqrt{3} \approx 0.90 \), the “close packing” fraction; \( \phi_f = 0.69 \), the “freezing” packing fraction; and \( \phi_c = 0.82 \), the “random close” packing fraction [5]. It should be noted that in one dimension, all three of these packing fractions are equal to 1; therefore, if we were to find that in two dimensions any one of these fractions is the desired factor, the theory would limit nicely to the lower dimensional result.

Since all the proposed excluded volumes above are of the form \( V = fNa \), with \( f \) the inverse of a packing fraction, a reasonable quantity to visualize is the effective inverse packing fraction, \( f_e = V_e/Na \). Higher \( f_e \) is associated with looser packings, i.e. higher per-molecule excluded volume. The inverse “close packing” fraction is \( f_{cp} = 1/0.90 \approx 1.1 \); the inverse “freezing” packing fraction is \( f_f = 1.45 \); and the inverse “random close” packing fraction is \( f_c \approx 1.22 \).
The three parameters of the simulation are $N$, the number of molecules, $L$, the diameter of the circular container, and $l$, the diameter of the molecules. In each of the plots in Figure 8, we keep two of these parameters fixed and vary the other. In the left plots we show $V_e$ (solid line), as estimated from solving Eq. (4), along with $V_d = Na$ for comparison (dashed line). In the right plots we show $f_e$. Note that $f_e$ is the ratio of the solid and dashed lines from the left plots.

The first two left plots (in which we vary $N$ and $l$) show that the effective excluded volume is higher than just the disk volume, as expected. But does the effective excluded volume correspond to some packing fraction? The first two plots on the right address just that question: it seems that no constant packing fraction can account for the effective excluded volume we observe, across the whole range of area densities and populations. The effective inverse packing fraction, $f_e$, decreases with increasing area density and with increasing population (see Figures 7b and 7c, as well, for a speculative result based on the pre-stirring initialization of positions).

This implies that the excluded volume situation for finite, reflective boundary containers is not as simple in two dimensions as it is in one dimension. Since the effective excluded volume is a function of the mean $\mu_e$ of the empirical $\tau$ -distribution (Eq. 4), the reason why the packing appears more compact as the number of molecules increases must relate back to the $\tau$ -distribution. But we have already shown that in situations with low population, the $\tau$ -distribution contains artifacts introduced by the reflective boundary, which ruin its exponentiality, and which obviously impact its mean. So it is reasonable
that in situations where the \( \tau \) -distribution is not exponential, the packing estimated from the empirical is surprising, in this case for its looseness.

At high population and intermediate density, e.g. \( N=20 \) and area density \( \sim12\% \), at the right end of Figure 8b, the packing reaches \( \phi_e = 1.8 \). At high population and high area density (\textit{but} simulated with pre-stirring), e.g. \( N=50 \) and area density \( \sim42\% \), at the right end of Figure 7c, the packing reaches \( \phi_e = 1.45 \), the freezing packing fraction. So, it appears that for densities at which the excluded area is a significant portion of the area of the system, at high population, the effective excluded area is reasonably close to close packed.

5. SUMMARY AND DISCUSSION

We have used computer simulations of hard disk dynamics to study the effect of reactant size on the rates of intermolecular collisions in the ballistic setting. We have found that the distribution of collision rates is close to exponential. It can be thought of as mostly exponential, except at low population, where we observe an additional mode which depends on the area density of the system.

At low population and low area density, non-ergodic trajectories contribute to longer than expected intermolecular collision times. At low population and high area density shorter intermolecular collision times are over-represented. We conclude, on the basis of exact
simulations, that increasing the population abolishes the low area density effect; on the basis of approximate simulations, we speculate that the same is true at high area density.

At intermediate and high area densities, the volume excluded by the reactants ranges from about 2.5 times the area of the molecules’ disks, at low population or low area density, to near the close packed volume, at high population or high area density.

In spite of differences in the details of the formula for the effective excluded volume in different population and area density regimes, it is clear that the probability of collision, and hence the reaction’s propensity function, will be higher in a system with large molecules, compared to a system with the same number but smaller molecules.

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REFERENCES

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[1] For an overview of relevant contributions to the development of the chemical master equation and the stochastic simulation algorithm, see the review article by D. Gillespie in Annu. Rev. Phys. Chem. 58, 35 (2007) and references therein.


FIGURE CAPTIONS

FIG 1: The mean of the $\tau$ -distribution, as calculated from simulations initialized with rejection-based Monte Carlo, is given by the solid lines. The dashed lines give the 95% confidence interval in the estimate of the mean. The circles and error bars give the means and 95% confidence intervals of the means of the $\tau$ -distribution, as calculated from simulations initialized with pre-stirring with $F$ given by the respective x-coordinates. The system is $N=9$, $L=10$, $l=2$.

FIG 2: To calculate the probability of collision of two randomly chosen molecules of diameter $l$, moving with relative velocity $v_{\text{rel}}$, in the next infinitesimal time $dt$ we compute the area that one molecule sweeps relative to the other in that amount of time: $2ls_{\text{rel}}dt$.

FIG 3: Results of K-S test for exponentiality of the $\tau$ -distribution at significance level $\alpha = 0.05$, superimposed on a grayscale plot of the quantity $I_\tau = (\sigma_\tau/\mu_\tau)^{-1}$. The population is $N = 6$ for all samples; the standard deviation of the Cartesian velocity components is $\sigma = 1$ for all samples; the vertical axis is $l$, the diameter of one molecule, and the horizontal axis is $L$, the diameter of the system. ‘+’ denotes a $\tau$ -distribution which is indistinguishable from exponential ($p$-value > 0.05), while ‘o’ denotes a $\tau$ -distribution which deviates from the exponential ($p$-value < 0.05). Positive $I_\tau$ values
imply a distribution with more spread than an exponential, while negative values imply a
distribution with less spread than an exponential.

**FIG 4:** Piecewise histogram of the $\tau$ distribution for $\sigma = 1, N = 6, L = 35, l = 0.1$ vs
analytical pdfs of two exponentials. The dotted exponential has the same mean as the $\tau$
distribution (~191). The dashed exponential is the most conservative theoretical
prediction (with $V_e = V_d = Na$, where $a$ is the area of one molecule).

**FIG 5:** Piecewise histogram of the $\tau$ distribution for $\sigma = 1, N = 6, L = 10, l = 2.8$ vs
analytical pdfs of two exponentials. The dotted exponential has the same mean as the $\tau$
distribution (~0.1511). The dashed exponential is the most conservative theoretical
prediction (with $V_e = V_d = Na$, where $a$ is the area of one molecule).

**FIG 6:** Plot of the indicator $I_\tau = (\sigma_\tau / \mu_\tau) - 1$ for fixed low area density 0.5%, $L=10$, and
varying $N$. ‘+’ denote $\tau$ -distributions which are indistinguishable from exponential
according to the K-S test at significance 0.05, while ‘o’ denote $\tau$ -distributions which are non-exponential.

**FIG 7:** (6a) Plot of the exponentiality according to the K-S test, and the indicator
$I_\tau = (\sigma_\tau / \mu_\tau) - 1$ for fixed high area density ~42%, $L=10$, and varying $N$. ‘+’ denote $\tau$ -
distributions which are indistinguishable from exponential, according to the K-S test at
significance 0.05, while ‘o’ denote $\tau$ -distributions which are not exponential by the K-S
test. The y-coordinate of the ‘+’ and ‘o’ gives the $I_e$ value for each distribution. Plot of the effective excluded volume $V_e$ (7b), and inverse packing fraction $f_e$ (7c), as a function of $N$, for the same fixed high area density $\sim 42\%$, and $L=10$. The dashed line in (7b) gives $V_d = Na$.

**FIG 8:** Plots of the effective excluded volume $V_e$ (left) and inverse packing fraction $f_e$ (right), as a function of the three parameters $L$, $l$, and $N$, keeping two parameters fixed, and varying the other. For all plots we have $\sigma = 1$, ensembles of size 100,000, and 95% confidence intervals. The dashed lines give $V_d = Na$. In the top plots we vary $N$, the number of disks, while maintaining $L=35$, $l=2.8$; in the middle plots we vary $l$, the diameter of the molecule disks, while maintaining $N=6$, $L=10$; in the bottom plots we vary $L$, the diameter of the container circle, while maintaining $N=6$, $l=2.8$. 
Figure 1
Figure 2
Figure 3
Figure 4
Figure 5

- **MD simulation data**
- **Exponential with mean of data**
- **Theoretical exponential (conservative)**

**Graph Details:**
- **Y-axis:** Probability density (time\(^{-1}\))
- **X-axis:** $\tau$

**Graph Notes:**
- The graphs show the comparison between MD simulation data, exponential fit with the mean of data, and the theoretical exponential fit (conservative).

**Legend:**
- The legend explains the different lines and their respective meanings in the context of the graphs.
Figure 6
Figure 7
Figure 8