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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.

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 (for an overview of relevant contributions to the development of the chemical master equation and the stochastic simulation algorithm, see the review article [1] and references therein). In the thermodynamic limit

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(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 τ 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 $A + A \rightarrow products$ in a one-dimensional system of N non-overlapping hard rods of length l moving ballistically in a volume of length L:

$$p_{\mathrm{col}}(dt) = \frac{N(N-1)s_{\mathrm{rel}}}{2(L-Nl)}\,dt. \tag{1}$$

(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_{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 disk system has proved to be challenging. The difficulty arises when trying to find an analytical inter-molecular 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 *computationally* investigate the effect of molecule size on the propensity for the $A + A \rightarrow products$ 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 non-zero 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 τ 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 τ in this system is approximately exponential, but with noticeable deviations in certain circumstances. We study how the τ 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 τ 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 over-represented; as the area density of the system becomes high, *short* inter-molecular collision times are over-represented.

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 τ distribution for short