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# TRACKABLE SPECIES DYNAMICS IN REACTION NETWORK MODELS\*

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**Abstract.** In a stochastic reaction network setting we define a subset of species as 'trackable' if we can consistently follow the fate of its individual molecules. We show that using the classical large volume limit results, we may approximate the dynamics of a single molecule of trackable species in a simple and computationally efficient way. We give examples on how this approach may be used to obtain various characteristics of single-molecule dynamics (for instance, the distribution of the number of infections in a single individual in the course of an epidemic or the activity time of a single enzyme molecule). Moreover, we show how to approximate the overall dynamics of trackable species in the full system with a collection of independent single-molecule trajectories, and give explicit bounds for the approximation error in terms of the reaction rates. This approximation, which is well defined for all times, leads to an efficient and fully parallelizable simulation technique for which we provide some numerical examples.

**Key words.** Single-molecule dynamics, mathematical epidemiology, law of large numbers, Poisson process representation, stochastic approximation, dynamic survival analysis, Skorohod topology

**AMS subject classifications.** 60J28, 92C40, 92C42, 60F05

**1. Introduction.** Recent advances in modeling molecular systems, especially our improved ability to track individual proteins, and the deluge of data from the observations of both molecular and macro system (think, for instance, of the ongoing COVID-19 pandemic), have created new scientific challenges of considering models of very high resolution where the dynamics of a specific bio-molecule or a particular individual are of interest. In general, such 'agent-based' models are known to be computationally very costly, due to complex stochastic dynamics and highly noisy behavior of individual agents. However, it appears that, at least in some cases, simple yet satisfactory approximation of individual molecular trajectory may be directly inferred with the help of a classical approach of stochastic chemical kinetics that assumes that all molecules or individuals are indistinguishable and consequently focuses only on their aggregated counts. As an example of one such idea, originally proposed in [7] and latter expanded in [15], consider the stochastic 'susceptible-infected' ( $SI$ ) chemical reaction network where a collection of  $m + n$  molecules (or individuals) is partitioned into two types: susceptible ( $S$ ) and infected ( $I$ ) with initially  $n$  being of type  $S$  and remaining  $m$  of type  $I$ . The stochastic network evolves in time according to a Markov jump process that counts the 'infection events', that is, the interactions of one molecule of  $I$ -type with one molecule of  $S$ -type. Each such interaction creates a new molecule of  $I$ -type and removes one of  $S$ -type (equivalently, a molecule changes its type from  $S$  to  $I$ ). Accordingly, in the reaction network notation described below in Section 2.2 this model may be represented as



If the rate constant of the above reaction is  $\beta/n$  and we assume the usual mass action kinetics [6], it is well known that the above stochastic reaction network satisfies the

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42 law of large numbers (admits the fluid limit approximation), in the sense that as  
 43  $m, n \rightarrow \infty$  and  $m/n \rightarrow \rho > 0$  the surviving proportion  $s_t$  of the  $S$ -type molecules  
 44 follows the logistic equation that may be written in the form

$$45 \quad (1.2) \quad -\dot{s}_t/s_t = \beta(1 + \rho - s_t) \quad s_t(0) = 1.$$

46 Consequently, for  $t \geq 0$  we have

$$47 \quad (1.3) \quad s_t = \frac{1 + \rho}{1 + \rho \exp(\beta(1 + \rho)t)}.$$

48 Thus, from the viewpoint of a single, randomly selected  $S$ -type molecule, the quantity  
 49  $s_t$  defines a *survival function* describing the limiting *probability* of surviving beyond  
 50 time  $t > 0$ . The formula (1.3) led to the method of approximating the distribution  
 51 of surviving molecules of  $S$  dubbed 'dynamic survival analysis' (DSA) described in  
 52 [15] and applied recently to epidemic modeling [8, 9, 14, 21, 23]. The idea is further  
 53 illustrated in Figure 1 where the average of the Markov process (1.1) is compared to  
 54 the average of independent realizations of single molecule dynamics (which may be  
 55 efficiently calculated using modern parallel computing capabilities). Note (1.2) may  
 56 be also interpreted as the equation for the *hazard function* associated with  $s_t$ . This  
 57 fact has some relevance for statistical inference, and is further exploited, for instance,  
 58 in [9, 15].

59 Beyond the simple  $SI$  example, the DSA approach has been applied (mostly in  
 60 the context of epidemics) only to a handful of reaction networks representing the so-  
 61 called one-directional transfer models [7]. In all such networks individual molecules  
 62 can only change their state in an ordered way, hence previously visited states are no  
 63 longer attainable (for instance in the  $SI$  model a molecule of  $S$ -type can only change  
 64 into  $I$ -type, but not vice-versa).

65 In the current paper we formally expand the survival function approach for track-  
 66 ing the fate of individual molecules to a much broader class of networks, including  
 67 those where molecules can return to their previous stages. A simple example is ob-  
 68 tained by augmenting the  $SI$  network with the additional reaction  $I \rightarrow S$ , leading  
 69 to the so-called  $SIS$  model (which is of interest in epidemiology) discussed in more  
 70 detail in Example 4.3 below. To establish our results for such networks, we explore a  
 71 different representation of the DSA approximation, which does not explicitly involve  
 72 the survival function. Continuing with the  $SI$  model example, denote by  $Y^i(t)$  the  
 73 binary variable that takes value 1 or 0 according to whether  $i$ -th molecule is of type  
 74  $S$  or  $I$ . The limit dynamics of an  $i$ -th individual molecule (initially of type  $S$ ) is then  
 75 given by

$$76 \quad Y^i(t) = 1 - N^i \left( \beta \int_0^t Y^i(u)(1 + \rho - s_u) du \right)$$

77 where  $N^i$  is the unit Poisson process tracking the transition of the  $i$ -th molecule  
 78 from  $S$ -type to  $I$ -type. Note that the argument of  $N^i$  is the cumulative hazard  
 79 corresponding to integral of the right-hand side of (1.2) (see [15]). Such Poisson  
 80 process representation is of course completely equivalent to simply having the time  
 81 of switching of the  $i$ -th molecule from  $S$  to  $I$  follow the survival function (1.3), but  
 82 it allows for a description of more complex scenarios than one-directional transfer  
 83 models. For example, we will prove below that the limit dynamics of a single molecule

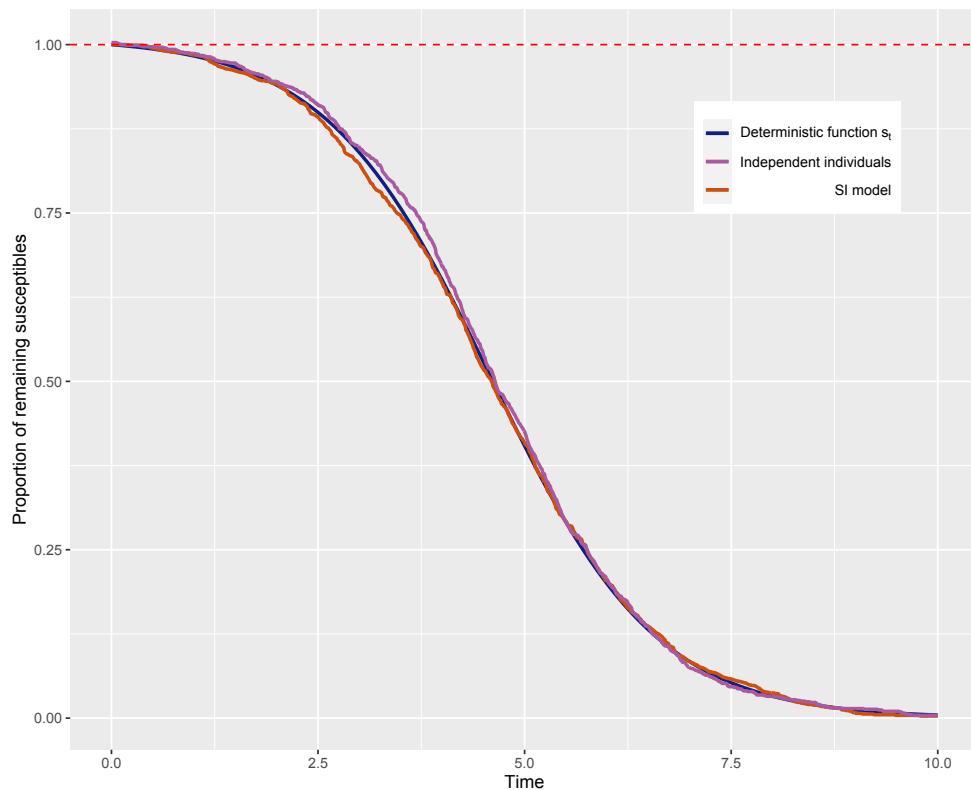


FIG. 1. **Survival approximation in the SI model.** The empirical trajectory of the proportion of the remaining  $S$  molecules in the SI model described in (1.1) as compared to the deterministic function  $s_t$  defined in (1.2) and the average of 1,000 independent single trajectories of individuals who become infected according to  $s_t$ . For the simulation we considered  $n = 1,000$ ,  $m = 10$ ,  $\beta = 1$ , and  $\rho = 0.01$ .

84 in the  $SIS$  model can be written as

$$85 \quad Y^i(t) = 1 - N_1^i \left( \beta \int_0^t Y^i(u)(1 + \rho - s_u) du \right) + N_2^i \left( \kappa \int_0^t (1 - Y^i(u)) du \right)$$

86 for independent and identically distributed unit-rate Poisson processes  $N_1^i$  and  $N_2^i$ .  
87 Here,  $\kappa$  is the rate constant of the reaction  $I \rightarrow S$ .

88 In this work we study the Poisson process representation of the DSA approxima-  
89 tion and give conditions under which it describes a single-molecule trajectory of the  
90 original network. In particular, we explicitly derive error bounds of the DSA approxi-  
91 mation, in terms of the underlying reaction network rates. We illustrate via numerical  
92 examples how this novel technique could be useful to infer quantities pertaining to  
93 single-molecule dynamics (such as the distribution of the number of infections a single  
94 individual undergoes in a  $SIS$  model, or the time a single enzyme spends in the bound  
95 state) in a computationally efficient way.

96 Further, we consider the problem of comparing the dynamics of an original full  
97 reaction network with that of a collection of independent approximations of single-

98 molecule trajectories and provide explicit bounds on the error. Having the dynamics  
 99 of the whole system approximated by a number of independent trajectories allows for  
 100 computationally efficient simulation techniques, that are fully parallelizable. More-  
 101 over, since the DSA approximation is defined for all times, it does not suffer from the  
 102 problem of exiting the state space as it is known to happen in other methods such  
 103 as diffusion approximations or tau leaping [4, 5, 12, 18]. Finally, the independence of  
 104 the single-molecule trajectories also allows for much simplified statistical inferential  
 105 procedures. Such applications were already considered in the context of SIR networks  
 106 in recent papers on the Covid pandemic [14, 23]. A thorough investigation of these  
 107 techniques in general reaction networks is currently being conducted and will appear  
 108 in a future work.

109 The paper is organized as follows: in Section 2 we provide the necessary concepts  
 110 pertaining to reaction network theory followed by the result on the approximation in  
 111 classical scaling in Section 3. In Section 4 we give a formal definition of single-molecule  
 112 trajectories of what we refer to as species that are 'trackable'. In Section 5 we state  
 113 our main results. In particular, in Section 5.1 we give the theorem on the Poisson  
 114 process representation of the DSA approximation for a single-molecule trajectory,  
 115 and give examples of its applications in Section 5.2. Finally, in Section 5.3 we state  
 116 the result on the approximation of the original full network via independent single-  
 117 molecule trajectories, and give numerical examples. Proofs and explicit error bounds  
 118 are given in the Appendix A.

## 119 2. Background definitions.

120 **2.1. Notation.** We denote by  $\mathbb{R}$ ,  $\mathbb{R}_{>0}$ , and  $\mathbb{R}_{\geq 0}$  the real, positive real, and non-  
 121 negative real numbers, respectively. Similarly, we denote by  $\mathbb{Z}$ ,  $\mathbb{Z}_{\geq 1}$ , and  $\mathbb{Z}_{\geq 0}$  the real,  
 122 positive real, and non-negative real numbers, respectively. Given a number  $r \in \mathbb{R}$ , we  
 123 denote by  $|r|$  its absolute value, and by  $\lfloor r \rfloor$  the largest  $m \in \mathbb{Z}$  such that  $m \leq r$ .

124 Given a vectors  $v \in \mathbb{R}^n$ , we denote its  $i$ th component by  $v_i$ , for all  $1 \leq i \leq n$ . We  
 125 further denote

$$126 \quad \|v\|_{\infty} = \max_{1 \leq i \leq n} |v_i| \quad \text{and} \quad \lfloor v \rfloor = (\lfloor v_1 \rfloor, \dots, \lfloor v_n \rfloor).$$

127 Given two vectors  $u, v \in \mathbb{R}_{\geq 0}^n$ , we write

$$128 \quad u^v = \prod_{i=1}^m u_i^{v_i},$$

129 with the convention that  $0^0 = 1$ . We also write  $u \geq v$  if the inequality holds  
 130 component-wise. Furthermore, for any vector  $v \in \mathbb{Z}_{\geq 0}^n$ , we write

$$131 \quad v! = \prod_{i=1}^m v_i!.$$

132 Given a set  $A$ , we denote its cardinality by  $\#A$  or, if it leads to no ambiguity, by  $|A|$ .  
 133 We assume the reader is familiar with basic notions from stochastic process theory,  
 134 such as the definition of continuous-time Markov chains and Poisson processes [19].

135 Consider a sequence of random variables  $\{X_n\}_{n \in \mathbb{Z}_{\geq 0}}$  and a random variable  $X$ ,  
 136 all defined on the same probability space and with values in a normed space  $(E, \|\cdot\|)$ .

137 We say that  $X_n$  converges in probability to  $X$  if for all  $\eta \in \mathbb{R}_{>0}$

$$138 \quad \lim_{n \rightarrow \infty} P(\|X_n - X\| > \eta) = 0.$$

139 Given a topological space  $E$  we will denote by  $D_E[0, T]$  the set of right-continuous  
 140 left-bounded functions defined from  $[0, T]$  to  $E$ , endowed with the Skorohod  $J_1$  topol-  
 141 ogy. In particular, we say that the sequence of processes  $\{X_n\}$  with sample paths  
 142 in  $D_E[0, T]$  converges in probability to the process  $X$  (or simply that  $X_n$  converges  
 143 in probability to  $X$ ) if the Skorohod distance between  $X_n$  and  $X$  converges to 0 in  
 144 probability (for more details, see for example [11, Chapter 3]).

145 **2.2. Stochastic reaction networks.** A *reaction network* is a triple  $\mathcal{G} = \{\mathcal{X}, \mathcal{C}, \mathcal{R}\}$  ■  
 146 where (a)  $\mathcal{X}$  is an ordered finite sequence of  $d$  symbols, called *species*; (b)  $\mathcal{C}$  is a finite  
 147 set of linear combinations of species over  $\mathbb{Z}_{\geq 0}$ , called *complexes*; (c)  $\mathcal{R}$  is a finite set  
 148 of elements of  $\mathcal{C} \times \mathcal{C}$ , called *reactions*. We assume that no element of the form  $(y, y)$  is  
 149 in  $\mathcal{R}$ , for any complex  $y$ , even though our results do not depend on this assumption.  
 150 Following the usual notation of reaction network Theory, we further denote a reaction  
 151  $(y, y') \in \mathcal{R}$  by  $y \rightarrow y'$ . We finally assume that each complex appears in at least  
 152 one reaction, and that each species has a positive coefficient in at least one complex.  
 153 Under this assumption and up to ordering of the set of species, a reaction network is  
 154 uniquely determined by the set  $\mathcal{R}$ , or equivalently by the directed graph  $(\mathcal{C}, \mathcal{R})$ , called  
 155 *reaction graph*. As an example, consider the reaction graph



157 In this case, the associated species are  $A$ ,  $B$ , and  $C$ ,  $\mathcal{C} = \{A + B, 2B, B, C\}$ , and  
 158  $\mathcal{R} = \{A + B \rightarrow 2B, 2B \rightarrow A + B, B \rightarrow C\}$ .

159 In this paper we will implicitly identify  $\mathbb{R}^{|\mathcal{X}|}$  with  $\mathbb{R}^d$ , and therefore each  $S \in \mathcal{X}$   
 160 with a canonical basis vector of  $\mathbb{R}^d$ . With this in mind, the complexes are linear  
 161 combination of species and can be therefore considered as vectors in  $\mathbb{Z}_{\geq 0}^d$ . As an  
 162 example, if we order the species of (2.1) alphabetically, then the complex  $A + B$  can be  
 163 associated with the vector  $(1, 1, 0)$ , the complex  $2B$  can be associated with  $(0, 2, 0)$ , the  
 164 complex  $C$  with  $(0, 0, 1)$ , and so on. We will tacitly use the identification of complexes  
 165 with integer vectors throughout the paper. Moreover, for each vector  $v \in \mathbb{R}^d$  and for  
 166 each species  $S \in \mathcal{X}$  we denote by  $v_S$  the entry of  $v$  related to the canonical vector  
 167 associated with  $S$ . We further define the *support* of  $v$  as  $\text{supp}(v) = \{S \in \mathcal{X} : v_S > 0\}$ .  
 168 As an example, with the species of (2.1) alphabetically ordered, the support of  $(1, 1, 0)$   
 169 is  $\{A, B\}$ , the support of  $(0, 2, 0)$  is  $\{B\}$ , and so on.

170 Deterministic and stochastic dynamical systems can be associated with a reaction  
 171 network. The stochastic model is usually utilized when few individuals are present,  
 172 so the stochastic component of the dynamic behaviour should not be ignored. In  
 173 this case, the time evolution of the number of individuals of the different species is  
 174 considered, for certain given propensities of the reactions to occur, and modeled via  
 175 a continuous time Markov chain. More precisely, a *stochastic kinetics* for a reac-  
 176 tion network  $\mathcal{G}$  is a correspondence between a reaction  $y \rightarrow y'$  and a *rate function*  
 177  $\lambda_{y \rightarrow y'} : \mathbb{Z}_{\geq 0}^d \rightarrow \mathbb{R}_{\geq 0}$ , such that  $\lambda_{y \rightarrow y'}(x) > 0$  only if  $x \geq y$ . A *stochastic reaction*  
 178 *system* is a continuous time Markov chain  $\{X(t) : t \geq 0\}$  with state space  $\mathbb{Z}_{\geq 0}^d$  and  
 179 transition rates from a state  $x$  to a state  $x'$  defined by

$$180 \quad q(x, x') = \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' - y = x' - x}} \lambda_{y \rightarrow y'}(x).$$

181 The associated generator is defined by

$$182 \quad Af(x) = \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x) (f(x + y' - y) - f(x))$$

183 for any function  $f: \mathbb{Z}_{\geq 0}^d \rightarrow \mathbb{R}$  and any  $x \in \mathbb{Z}_{\geq 0}^d$ . Equivalently, the process  $X$  can be  
184 described by

$$185 \quad X(t) = X(0) + \sum_{y \rightarrow y' \in \mathcal{R}} (y' - y) N_{y \rightarrow y'} \left( \int_0^\infty \lambda_{y \rightarrow y'}(X(s)) ds \right),$$

186 where the processes  $\{N_{y \rightarrow y'}\}_{y \rightarrow y' \in \mathcal{R}}$  are independent unit-rate Poisson processes. For  
187 more details on this representation, we refer to [6] or [11, Chapter 6].

188 In the deterministic setting, the concentration of the different species are assumed  
189 to evolve according to an ordinary differential equation (ODE). Specifically, a *deter-*  
190 *ministic kinetics* for a reaction network  $\mathcal{G}$  is a correspondence between the reactions  
191  $y \rightarrow y'$  and the *rate function*  $\lambda_{y \rightarrow y'}: \mathbb{R}_{\geq 0}^d \rightarrow \mathbb{R}_{\geq 0}$ , such that  $\lambda_{y \rightarrow y'}(x) > 0$  only  
192 if  $x_i > 0$  whenever  $y_i > 0$ . A *deterministic reaction system* is the solution to the  
193 ordinary differential equation

$$194 \quad (2.2) \quad \frac{d}{dt} Z(t) = \sum_{y \rightarrow y' \in \mathcal{R}} (y' - y) \lambda_{y \rightarrow y'}(x).$$

195 While our results hold in a more general scenario, all the simulations we show as-  
196 sume *mass-action kinetics*, a popular choice of kinetics derived by the assumption that  
197 all the reactants are well-mixed in the available volume [6]. Specifically, a stochastic  
198 reaction system is a *stochastic mass-action system* if for every reaction  $y \rightarrow y' \in \mathcal{R}$   
199 we have

$$200 \quad \lambda_{y \rightarrow y'}(x) = \kappa_{y \rightarrow y'} \frac{x!}{(x - y)!} \mathbb{1}_{\{x \geq y\}},$$

201 for some positive constant  $\kappa_{y \rightarrow y'}$  called *rate constant*. Similarly, a deterministic re-  
202 action system is a *deterministic mass-action system* if for every reaction  $y \rightarrow y' \in \mathcal{R}$   
203 we have

$$204 \quad \lambda_{y \rightarrow y'}(x) = \kappa_{y \rightarrow y'} x^y,$$

205 for some positive constant  $\kappa_{y \rightarrow y'}$  also called *rate constant*.

206 **3. Classical scaling.** Consider a reaction network  $\mathcal{G} = \{\mathcal{X}, \mathcal{C}, \mathcal{R}\}$ , and a family  
207 of stochastic kinetics  $\{\lambda_{y \rightarrow y'}^V : y \rightarrow y' \in \mathcal{R}\}$  indexed by  $V$ . Let  $X^V$  denote the  
208 associated continuous time Markov chain.  $V$  should be thought to as a parameter  
209 expressing the volume, or the magnitude of the number of the present individuals.  
210 Under the following technical but reasonable assumption the classical scaling of [11, 16]  
211 holds:

212 *Assumption 3.1.* We assume that for any reaction  $y \rightarrow y' \in \mathcal{R}$  there exists a  
213 locally Lipschitz function  $\lambda_{y \rightarrow y'}: \mathbb{R}_{\geq 0}^d \rightarrow \mathbb{R}_{\geq 0}^d$  such that for any compact set  $K \subset \mathbb{R}_{\geq 0}^d$   
214 we have

$$215 \quad \lim_{V \rightarrow \infty} \sup_{z \in K} \left| \frac{\lambda_{y \rightarrow y'}^V([Vz])}{V} - \lambda_{y \rightarrow y'}(z) \right| = 0.$$

216 THEOREM 3.2. Assume that Assumption 3.1 holds. Furthermore, assume that  
 217 the random variables  $X^V(0)/V$  converge in probability to a constant  $z^*$  as  $V$  goes to  
 218 infinity. Finally, let  $\{Z(t) : t \geq 0\}$  be the unique solution to (2.2) with  $Z(0) = z^*$ .  
 219 Then, for any  $\varepsilon > 0$  and any  $T > 0$

$$220 \quad \lim_{V \rightarrow \infty} P \left( \sup_{t \in [0, T]} \left\| \frac{X^V(t)}{V} - Z(t) \right\|_{\infty} > \varepsilon \right) = 0.$$

221 Note that the distribution of the fate of a single molecule is not given, since the  
 222 classical scaling concerns average dynamics. The goal of this paper is to address this  
 223 issue, by providing a technique to simulate an approximation of the time evolution of  
 224 a single observable species, as described in the next section.

225 **4. Trackable species.** We consider a special set of reactants, and assume that  
 226 we can consistently follow the fate of a single molecule of these reactants through its  
 227 different transformations, as for a single individual in the SI model. In general, the  
 228 reactants whose dynamics we want to follow may be less than the chemical species  
 229 listed in  $\mathcal{X}$ , or may be *portions* of them as in Example 4.5 below. To deal with this  
 230 general setting, we introduce the set of *trackable species* as a set  $\tilde{\mathcal{X}}$  of symbols endowed  
 231 with a function  $\tau: \tilde{\mathcal{X}} \rightarrow \mathcal{X} \cup \{0\}$ . The different trackable species will identify the  
 232 possible states of the molecules whose fate we want to follow. Every such state is taken  
 233 by the reactant molecule when the molecule is (part of) one of the chemical species  
 234 of  $\mathcal{X}$ . The function  $\tau$  will link every trackable species with the corresponding species  
 235 in  $\mathcal{X}$ . The number of trackable species defined in this way can be less than, equal to,  
 236 or larger than the number of species. The set  $\tilde{\mathcal{X}}$  needs to include the special state  
 237  $\Delta$  to denote the potential degradation of the tracked molecule, and we set  $\tau\Delta = 0$ .  
 238 To simplify the notation, for all  $x, y \in \mathbb{Z}_{\geq 0}^d$  and  $\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}$  we denote by  $\theta_y(\tilde{S}, x)$   
 239 the probability that a certain molecule of species  $\tau(\tilde{S})$  is chosen if  $y_{\tau(\tilde{S})}$  molecules are  
 240 uniformly drawn out of  $x_{\tau(\tilde{S})}$  molecules of  $\tau(\tilde{S})$  available. Specifically,

$$241 \quad \theta_y(\tilde{S}, x) = \begin{cases} \frac{\binom{x_{\tau(\tilde{S})} - 1}{y_{\tau(\tilde{S})} - 1}}{\binom{x_{\tau(\tilde{S})}}{y_{\tau(\tilde{S})}}} = \frac{y_{\tau(\tilde{S})}}{x_{\tau(\tilde{S})}} & \text{if } x_{\tau(\tilde{S})} \geq y_{\tau(\tilde{S})} \geq 1 \\ 0 & \text{otherwise} \end{cases}.$$

242 For completeness, we define  $\theta_y(\Delta, x) = 0$ . Finally, note that in reactions such as  
 243  $2A \rightarrow B + C$  we can imagine a molecule of  $A$  is transformed into a molecule of  $B$ , while  
 244 the other molecule of  $A$  turns into a molecule of  $C$ . If we are tracking the fate of  $A$   
 245 molecules and the reaction  $2A \rightarrow B + C$  occurs, it is reasonable to assume the molecule  
 246 we are tracking has a 50% change of turning into a molecule of  $B$ , and a 50% change  
 247 of becoming a molecule of  $C$ . We denote these probabilities with  $p_{2A \rightarrow B+C}(A, B)$   
 248 and  $p_{2A \rightarrow B+C}(A, C)$ , respectively, and in general allow for different value choices, as  
 249 along as  $p_{2A \rightarrow B+C}(A, B) + p_{2A \rightarrow B+C}(A, C) = 1$ . The definition of *stochastic reaction*  
 250 *system with trackable species* in the most general setting is below.

251 DEFINITION 4.1 (Stochastic reaction system with trackable species). Let  $\mathcal{G} =$   
 252  $\{\mathcal{X}, \mathcal{C}, \mathcal{R}\}$  be a reaction network. Consider a family of stochastic kinetics  $\{\lambda_{y \rightarrow y'}^V : y \rightarrow y' \in \mathcal{R}\}$   
 253 indexed by  $V$ , and let  $X^V$  denote the associated continuous time Markov  
 254 chains. Let  $\tilde{\mathcal{X}}$  be a set of trackable species. We define the stochastic reaction system  
 255 with trackable species as the continuous-time Markov chain  $(Y^V, X^V)$  with state space

256  $\tilde{\mathcal{X}} \times \mathbb{Z}_{\geq 0}^d$  and transition rates

$$257 \quad q\left((\Delta, x), (\tilde{S}', x')\right) = \mathbb{1}_{\{\tilde{S}'\}}(\Delta) \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' - y = x' - x}} \lambda_{y \rightarrow y'}^V(x)$$

258  
259 and for all  $\tilde{S} \neq \Delta$

$$260 \quad q\left((\tilde{S}, x), (\tilde{S}', x')\right) = \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' - y = x' - x}} \left( (1 - \theta_y(\tilde{S}, x)) \mathbb{1}_{\{\tilde{S} = \tilde{S}'\}} + \theta_y(\tilde{S}, x) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \right) \lambda_{y \rightarrow y'}^V(x),$$

261  
262 where for all reactions  $y \rightarrow y' \in \mathcal{R}$  the following holds:

- 263 • for any  $\tilde{S} \in \tilde{\mathcal{X}}, \tilde{S}' \in \tilde{\mathcal{X}} \cup \{\Delta\}$  we have  $0 \leq p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \leq 1$ ;
- 264 •  $p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') = 0$  whenever  $\tau(\tilde{S}) \notin \text{supp}(y)$  or  $\tau(\tilde{S}') \notin \text{supp}(y') \cup \Delta$ ;
- 265 • if  $\tau(\tilde{S}) \in \text{supp}(y)$  then

$$266 \quad \sum_{\tilde{S}' \in \tilde{\mathcal{X}} : \tau(\tilde{S}') \in \text{supp}(y') \cup \Delta} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') = 1.$$

267 In the above definition, the usual stochastic reaction system is coupled with the  
 268 fate of a single trackable molecule: a trackable molecule in state  $\tilde{S}$  can transform  
 269 whenever a reaction  $y \rightarrow y'$  occurs, with a probability given by  $\theta_y(\tilde{S}, \tilde{S}')$ . By defini-  
 270 tion, the quantity  $\theta_y(\tilde{S}, \tilde{S}')$  denotes precisely the probability that the tracked molecule  
 271 takes part in the reaction  $y \rightarrow y'$ , assuming that the reacting molecules are uniformly  
 272 chosen among those present. If that happens, the new state of the tracked molecule is  
 273 drawn according to the probability distribution  $\{p_{y \rightarrow y'}(\tilde{S}, \tilde{S}')\}_{\tilde{S}' \in \text{supp}(y') \cup \Delta}$  (see Ex-  
 274 ample 4.4 for a case where this distribution is non-trivial). If the tracked molecule is  
 275 irreversibly degraded, its state becomes  $\Delta$  and cannot be changed. In what follows,  
 276 we will sometimes identify the state space of  $Y^V$ , given by  $\tilde{\mathcal{X}}$ , with the canonical basis  
 277 of  $\mathbb{R}^{|\tilde{\mathcal{X}}|}$ , similarly to how complexes are implicitly identified with vectors in  $\mathbb{R}^d$ .

278 The only technical requirement to have trackable species is that in every reaction,  
 279 every piece of the reactants on the left-hand side of the reaction either transforms  
 280 into a piece of the reactants on the right-hand side, or is discarded. Mathematically,  
 281 mapping the chemical species of the left-hand side of the reaction with those on the  
 282 right-hand side is always possible by mapping to  $\Delta$  potential species in excess on  
 283 the left-hand side, so in principle the requirements of Definition 4.1 can always be  
 284 satisfied with the choice  $\tilde{\mathcal{X}} = \mathcal{X}$  and  $\tau$  being the identity. Moreover, if we consider  
 285 the physical system modelled by the reaction network, it is always true that reactions  
 286 either transform molecules or degrade them. Hence, even when considering the phys-  
 287 ical meaning of the model, trackable species can always be defined to track the fate of  
 288 every molecule of particular interest. In this case however some care should be taken  
 289 to reflect the real physical changes caused by the reactions, and the set  $\tilde{\mathcal{X}}$  may need  
 290 to be different from  $\mathcal{X}$ , as in Example 4.5.

291 *Remark 4.2.* The generator of a stochastic reaction system with trackable species,  
 292 as defined in Definition 4.1, is given by

$$293 \quad \mathcal{A}f(\Delta, x) = \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}^V(x) \left( f(\Delta, x + y' - y) - f(\Delta, x) \right)$$

294 and for  $\tilde{S} \neq \Delta$

295

$$296 \quad \mathcal{A}f(\tilde{S}, x) = \sum_{y \rightarrow y' \in \mathcal{R}} (1 - \theta_y(\tilde{S}, x)) \lambda_{y \rightarrow y'}^V(x) \left( f(\tilde{S}, x + y' - y) - f(\tilde{S}, x) \right)$$

$$297 \quad + \sum_{y \rightarrow y' \in \mathcal{R}} \sum_{\tilde{S}' \in \text{supp}(y') \cup \Delta} \theta_y(\tilde{S}, x) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \lambda_{y \rightarrow y'}^V(x) \left( f(\tilde{S}', x + y' - y) - f(\tilde{S}, x) \right),$$

298

299 for all functions  $f: (\tilde{\mathcal{X}}) \times \mathbb{Z}_{\geq 0}^d \rightarrow \mathbb{R}$ .

300 *Example 4.3.* Consider the SI reaction network described in (1.1), which we re-  
301 peat here for convenience:

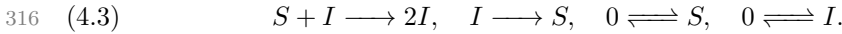


303 In this case, we are interested in describing the history of susceptible individuals  
304 who become infected. The set of trackable species is therefore  $\tilde{\mathcal{X}} = \{\tilde{S}, \tilde{I}\}$  with  
305  $\tau(\tilde{S}) = S$  and  $\tau(\tilde{I}) = I$ . Furthermore, we choose the probabilities  $p_{S+I \rightarrow 2I}(\tilde{S}, \tilde{I}) = 1$   
306 and  $p_{S+I \rightarrow 2I}(\tilde{I}, \tilde{I}) = 1$ . Alternatively, one can simply consider  $\tilde{\mathcal{X}} = \{\tilde{S}\}$ , with the  
307 understanding that whenever a susceptible individual gets infected we consider it as  
308 irreversibly degraded, and its state becomes  $\Delta$ . In this case,  $p_{S+I \rightarrow 2I}(\tilde{S}, \Delta) = 1$ .

309 The state of single individuals can be tracked also in the more complex model

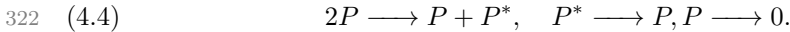


311 Here, the set of trackable species is  $\{\tilde{S}, \tilde{I}\}$ , with  $\tau(\tilde{S}) = S$  and  $\tau(\tilde{I}) = I$ , and the trans-  
312 formation probabilities are  $p_{S+I \rightarrow 2I}(\tilde{S}, \tilde{I}) = 1$ ,  $p_{S+I \rightarrow 2I}(\tilde{I}, \tilde{I}) = 1$ ,  $p_{I \rightarrow S}(\tilde{I}, \tilde{S}) = 1$ .  
313 Here, relevant questions on the fate of a single individual could concern, for exam-  
314 ple, the number of infections it undergoes in a given time, or after how long the  $n$ th  
315 infection occurs. We can even extend the model to include migrations, and obtain



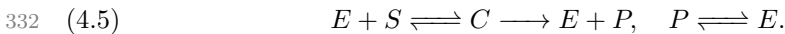
317 In this case, it is natural to assume  $p_{S \rightarrow 0}(\tilde{S}, \Delta) = 1$  and  $p_{I \rightarrow 0}(\tilde{I}, \Delta) = 1$ . Relevant  
318 questions could involve, for example, the average number of infection a susceptible  
319 individual undergoes before migrating.

320 *Example 4.4.* Consider the following reaction network, where a protein  $P$  pro-  
321 motes its own phosphorylation:



323 Here, we may assume we are interested in observing the dynamics of a molecule  
324 of protein  $P$ . Hence, the set of trackable species is  $\{\tilde{P}, \tilde{P}^*\}$  with  $\tau(\tilde{P}) = P$  and  
325  $\tau(\tilde{P}^*) = P^*$ . It is natural to assume that the two molecules of  $P$  involved in the  
326 reaction  $2P \rightarrow P + P^*$  have the same probability of being phosphorylated or serving as  
327 the reaction catalyst. Hence,  $p_{2P \rightarrow P+P^*}(\tilde{P}, \tilde{P}) = p_{2P \rightarrow P+P^*}(\tilde{P}, \tilde{P}^*) = 1/2$ . The other  
328 transformation probabilities are given by  $p_{P^* \rightarrow P}(\tilde{P}^*, \tilde{P}) = 1$  and  $p_{P \rightarrow 0}(\tilde{P}, \Delta) = 1$ .

329 *Example 4.5.* Consider the following reaction network, depicting a Michaelis-  
330 Menten mechanism where the product protein and the enzyme can spontaneously  
331 transform into each other:



333 In particular, the complex  $C$  represents a molecule of substrate  $S$  and enzyme bound  
 334 together. When the bound is broken, it is natural to assume that the molecule of  
 335 enzyme is released while the molecule of substrate is either released or transformed  
 336 into the product  $P$ . Suppose we want to keep track of the history of a molecule of  
 337 substrate  $S$ . If we were dealing with a classic Michaelis-Menten kinetics, i.e. without  
 338 the reactions  $P \rightleftharpoons E$ , then we could simply consider as trackable species  $S$ ,  $C$ , and  $P$   
 339 (or, more formally,  $S$ ,  $C$ , and  $P$  with  $\tau(\tilde{S}) = S$ ,  $\tau(\tilde{C}) = C$ , and  $\tau(\tilde{P}) = P$ ). Indeed, a  
 340 molecule of substrate can be either in free state ( $\tilde{S}$ ), bound with the enzyme ( $\tilde{C}$ ), or  
 341 transformed into a product ( $\tilde{P}$ ). Since the reactions  $P \rightleftharpoons E$  are present, if we want  
 342 to keep track of the fate of a molecule of substrate  $S$  we need to take into account  
 343 the fact that it can transform into an enzyme, so  $E$  becomes a possible state of the  
 344 molecule (more formally,  $\tilde{E}$  with  $\tau(\tilde{E}) = E$ ). The problem now is that we need to  
 345 differentiate between the portion of  $C$  that  $E$  and  $S$  get transformed into by the  
 346 reaction  $E + S \rightarrow C$ : the portion of  $C$  that  $E$  gets transformed into will become a free  
 347 enzyme again via the reaction  $C \rightarrow E + P$ , while the portion  $S$  gets transformed into  
 348 will become a product. In order to formally express these dynamics, we consider as set  
 349 of trackable species  $\{\tilde{E}, \tilde{S}, \tilde{P}, \tilde{C}_E, \tilde{C}_S\}$ , where  $\tilde{C}_E$  denotes we are tracking a molecule  
 350 of  $E$  bound in the complex  $C$ , while  $\tilde{C}_S$  denotes we are tracking a molecule of  $S$   
 351 bound in  $C$ . The function  $\tau$  associates every trackable species with its physical type:  
 352  $\tau(\tilde{E}) = E$ ,  $\tau(\tilde{S}) = S$ ,  $\tau(\tilde{P}) = P$ ,  $\tau(\tilde{C}_E) = C$ , and  $\tau(\tilde{C}_S) = C$ . The transformation  
 353 probabilities are given by

$$\begin{aligned}
 354 \quad p_{E+S \rightarrow C}(\tilde{E}, \tilde{C}_E) &= 1 & p_{C \rightarrow E+S}(\tilde{C}_E, \tilde{E}) &= 1 & p_{C \rightarrow E+P}(\tilde{C}_E, \tilde{E}) &= 1 \\
 p_{E+S \rightarrow C}(\tilde{S}, \tilde{C}_S) &= 1 & p_{C \rightarrow E+S}(\tilde{C}_S, \tilde{S}) &= 1 & p_{C \rightarrow E+P}(\tilde{C}_S, \tilde{P}) &= 1 \\
 p_{P \rightarrow E}(\tilde{P}, \tilde{E}) &= 1 & p_{E \rightarrow P}(\tilde{E}, \tilde{P}) &= 1 & &
 \end{aligned}$$

355 *Remark 4.6.* The interpretation of a stochastic reaction system with trackable  
 356 species is that of a regular stochastic reaction system with the subsequent transfor-  
 357 mations of a given particle being tracked. If the initial state  $Y^V(0)$  of the tracked  
 358 molecule is not present in the initial  $X^V(0)$ , that is if  $X_{\tau(Y^V(0))}^V(0) = 0$ , then the  
 359 initial condition of  $(Y^V, X^V)$  is not consistent with the interpretation of the process.  
 360 The process  $(Y^V, X^V)$  is still well-defined and its evolution can be studied, but its  
 361 interpretation is no longer valid. In order to obtain meaningful results, we therefore  
 362 tacitly assume that  $X_{\tau(Y^V(0))}^V(0) > 0$ , even if we do not require it formally.

363 **4.1. Representation as a regular stochastic reaction network.** In this  
 364 section we show how a reaction network with trackable species  $(Y^V, X^V)$  can be  
 365 realized as a regular stochastic reaction network with species set given by  $\tilde{\mathcal{X}} \sqcup \mathcal{X}$ ,  
 366 where  $\sqcup$  denotes a disjoint union. In particular, the state space is  $\mathbb{Z}_{\geq 0}^{|\tilde{\mathcal{X}}|} \times \mathbb{Z}_{\geq 0}^d$ , where  
 367 for convenience we consider the first coordinates to refer to  $\tilde{\mathcal{X}}$ , and the rest to the  
 368 species of the original process  $\mathcal{X}$ . We denote by  $(\tilde{x}, x)$  a generic state in  $\mathbb{Z}_{\geq 0}^{|\tilde{\mathcal{X}}|} \times \mathbb{Z}_{\geq 0}^d$ .  
 369 Consider the set of reactions  $\tilde{\mathcal{R}} \cup \mathcal{R}$  where

$$370 \quad \tilde{\mathcal{R}} = \{\tilde{S} + y \rightarrow \tilde{S}' + y' : y \rightarrow y' \in \mathcal{R}, \tilde{S}, \tilde{S}' \in \tilde{\mathcal{X}} \text{ and } p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') > 0\}$$

371 and endow them with the following reaction rates:

$$\begin{aligned}
 372 \quad \lambda_{y \rightarrow y'}^V(\tilde{x}, x) &= \sum_{\tilde{S} \in \tilde{\mathcal{X}}} \tilde{x}_{\tilde{S}} (1 - \theta_y(\tilde{S}, x)) \lambda_{y \rightarrow y'}^V(x) \\
 373 \quad \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\tilde{x}, x) &= \tilde{x}_{\tilde{S}} \theta_y(\tilde{S}, x) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \lambda_{y \rightarrow y'}^V(x). \\
 374
 \end{aligned}$$

375 Note that the second component of the process has the same transitions as  $X^V$ , with  
 376 exactly the same rates. Hence, we can safely denote the process associated with the  
 377 above stochastic reaction network by  $(\tilde{Y}^V, X^V)$ . Note that the quantity  $\sum_{\tilde{s} \in \tilde{\mathcal{X}}} \tilde{x}_{\tilde{s}}$   
 378 is conserved by all possible transitions. Hence, if we consider an initial condition  
 379  $(\tilde{Y}(0), X(0))$  with  $\sum_{\tilde{s} \in \tilde{\mathcal{X}}} \tilde{Y}_{\tilde{s}}(0) = 1$ , then at any time point  $t$  exactly one entry of the  
 380 vector  $\tilde{Y}(t)$  is 1, and the other entries are zero. It follows that there is a bijection  
 381 between the possible values of  $\tilde{Y}$  and  $\tilde{\mathcal{X}}$ , given by the function  $\text{supp}(\tilde{Y}(t))$ . In this  
 382 case, by identifying trackable species with vectors of the canonical basis of  $\mathbb{R}^{|\tilde{\mathcal{X}}|}$  as  
 383 already done in the paper for the species in  $\mathcal{X}$ , the transition rates can be equivalently  
 384 written as

$$385 \quad \lambda_{y \rightarrow y'}^V(\tilde{x}, x) = \sum_{\tilde{s} \in \tilde{\mathcal{X}}} \mathbb{1}_{\{\tilde{s}\}}(\tilde{x})(1 - \theta_y(\tilde{S}, x)) \lambda_{y \rightarrow y'}^V(x)$$

$$386 \quad \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\tilde{x}, x) = \mathbb{1}_{\{\tilde{s}\}}(\tilde{x}) \theta_y(\tilde{S}, x) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \lambda_{y \rightarrow y'}^V(x),$$

388 Hence, if  $\sum_{\tilde{s} \in \tilde{\mathcal{X}}} \tilde{Y}_{\tilde{s}}(0) = 1$  then the transitions and the rates of  $(Y^V, X^V)$  and  
 389  $(\tilde{Y}^V, X^V)$  coincide, and  $(Y^V, X^V)$  can be therefore realized as a stochastic reaction  
 390 network with an appropriate initial condition. In particular, we can write

(4.6)

$$391 \quad X^V(t) = X^V(0) + \sum_{y \rightarrow y' \in \mathcal{R}} (y' - y) N_{y \rightarrow y'} \left( \int_0^t \lambda_{y \rightarrow y'}^V(X^V(s)) ds \right)$$

(4.7)

$$392 \quad Y^V(t) = Y^V(0) + \sum_{y+\tilde{S} \rightarrow y'+\tilde{S}' \in \tilde{\mathcal{R}}} (\tilde{S}' - \tilde{S}) N_{y+\tilde{S} \rightarrow y'+\tilde{S}'} \left( \int_0^t \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(Y^V(s), X^V(s)) ds \right)$$

394 where  $N_r$  for  $r \in \mathcal{R} \cup \tilde{\mathcal{R}}$  are independent unit-rate Poisson processes. Note that with  
 395 the above writing, all the processes in the set  $\{(Y^V, X^V)\}_{V \in \mathbb{Z}_{\geq 1}}$  can be defined on  
 396 the same probability space.

397 **5. Results.** In this section we state the main results of the current paper and  
 398 their applications.

399 **5.1. Classical scaling for the fate of a single molecule.** In this section we  
 400 state a law of large number for the process  $Y^V$ . In order to do this, we consider a family  
 401 of stochastic reaction systems with trackable species  $(Y^V, X^V)$ , with  $V$  varying in the  
 402 integer numbers greater than one. We then assume that Assumption 3.1 is satisfied  
 403 for some locally Lipschitz functions  $\lambda_{y \rightarrow y'}$ , and denote by  $Z$  the solution to (2.2).  
 404 Hence, we know by Theorem 3.2 that  $V^{-1}X^V$  will converge to  $Z$  path-wise with the  
 405 uniform convergence topology over compact intervals of time, for  $V$  going to infinity.

406 In this section we express  $(Y^V, X^V)$  by means of independent unit-rate Poisson  
 407 processes, as in (4.6) and (4.7). With the notation introduced in the previous section  
 408 in mind, we have the following first technical result:

409 **LEMMA 5.1.** *Assume that Assumption 3.1 holds. Then, for any  $\tilde{S}+y \rightarrow \tilde{S}'+y' \in$   
 410  $\tilde{\mathcal{R}}$ , any  $w \in \tilde{\mathcal{X}}$ , and any compact set  $K \subset \mathbb{R}_{>0}^d$  we have*

$$411 \quad (5.1) \quad \lim_{V \rightarrow \infty} \sup_{z \in K} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(w, \lfloor Vz \rfloor) - \lambda_{y \rightarrow y'}(w, z) \right| = 0,$$

412 where the function  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'} : \tilde{\mathcal{X}} \times \mathbb{R}_{\geq 0}^d$  is defined as

$$413 \quad \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(w, z) = \mathbb{1}_{\{w\}}(\tilde{S}) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') y_{\tau(\tilde{S})} \frac{\lambda_{y \rightarrow y'}(z)}{z_{\tau(\tilde{S})}}$$

414 if both  $z_{\tau(\tilde{S})}$  and  $y_{\tau(\tilde{S})}$  are positive, and zero otherwise. Moreover, the function  
415  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}$  is locally Lipschitz if restricted to  $\tilde{\mathcal{X}} \times \mathbb{R}_{> 0}^d$ .

416 *Proof.* If  $y_{\tau(S)} = 0$ , then both  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V$  and  $\lambda_{y \rightarrow y'}$  are constantly zero,  
417 hence (5.1) holds. If  $y_{\tau(S)}$  is positive, then for all  $z \in K$  we have

$$418 \quad \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(w, [Vz]) - \lambda_{y \rightarrow y'}(w, z) \right| =$$

$$419 \quad \mathbb{1}_{\{w\}}(\tilde{S}) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \left| \theta_y(\tilde{S}, [Vz]) \lambda_{y \rightarrow y'}^V([Vz]) - y_{\tau(S)} \frac{\lambda_{y \rightarrow y'}(z)}{z_{\tau(S)}} \right|$$

422 Let  $m = \min_{z \in K} z_{\tau(\tilde{S})}$ , which is positive because  $K$  is a compact set contained in  $\mathbb{R}_{> 0}^d$ .  
423 If  $V$  is large enough such that  $Vm > y_{\tau(\tilde{S})}$  then

$$424 \quad \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(w, [Vz]) - \lambda_{y \rightarrow y'}(w, z) \right| =$$

$$425 \quad \mathbb{1}_{\{w\}}(\tilde{S}) p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') y_{\tau(S)} \left| \frac{\lambda_{y \rightarrow y'}^V([Vz])}{V \cdot (\lfloor Vz_{\tau(\tilde{S})} \rfloor / V)} - \frac{\lambda_{y \rightarrow y'}(z)}{z_{\tau(S)}} \right|$$

428 Hence, (5.1) follows from Assumption 3.1 and

$$429 \quad \max_{z \in K} \left| \frac{\lfloor Vz_{\tau(\tilde{S})} \rfloor}{V} - z_{\tau(\tilde{S})} \right| \leq \frac{1}{V}.$$

430 To conclude the proof, we only need to show that  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}$  restricted to  $\tilde{\mathcal{X}} \times \mathbb{R}_{> 0}^d$  is  
431 locally Lipschitz. However, this follows from it being the product (up to multiplication  
432 by a constant) of the two locally Lipschitz functions  $z \mapsto 1/z_{\tau(\tilde{S})}$  and  $\lambda_{y \rightarrow y'}$ .  $\square$

433 The main goal of this section is to prove a classical scaling limit for a single-  
434 molecule trajectory. To this aim, define the process  $Y$  by  
(5.2)

$$435 \quad Y(t) = Y(0) + \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} (\tilde{S}' - \tilde{S}) N_{\tilde{S}+y \rightarrow \tilde{S}'+y'} \left( \int_0^t \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(Y(s), Z(s)) ds \right).$$

436 Then, the following result holds, where we implicitly identify the states of  $Y^V$  and  $Y$   
437 with the canonical basis of  $\mathbb{R}^{|\tilde{\mathcal{X}}|}$ . Note that the assumption that all the components  
438 of the solution  $Z$  are strictly positive in the time interval  $[0, T]$  is made, but this is  
439 only a mild restriction to avoid unnecessary technicality, and is always verified under  
440 mass-action kinetics as long as  $Z(0) \in \mathbb{R}_{> 0}^d$  (see Remark 5.3). The proof of the result  
441 is postponed to Appendix A, where more precise bounds are given.

442 **THEOREM 5.2.** *Assume that Assumption 3.1 holds. Furthermore, assume that*  
443 *the random variables  $X^V(0)/V$  converge in probability to some  $z^* \in \mathbb{R}_{> 0}^d$  as  $V$  goes*  
444 *to infinity, and let  $Z(0) = z^*$ . Assume that the solution  $Z$  to (2.2) with  $Z(0) = z^*$*

445 exists over the interval  $[0, T]$  and that

$$446 \quad m = \min_{\substack{i=1,2,\dots,d \\ u \in [0, T]}} Z_i(u) > 0.$$

447 Finally, assume that  $Y^V(0) = Y(0)$  for all positive integers  $V$ . Then

$$448 \quad (5.3) \quad \lim_{V \rightarrow \infty} \sup_{t \in [0, T]} P(Y^V(t) \neq Y(t)) = \lim_{V \rightarrow \infty} \sup_{t \in [0, T]} E[\|Y^V(t) - Y(t)\|_\infty] = 0.$$

449 *Remark 5.3.* If we consider mass-action kinetics, then the deterministic solutions  
 450 never touch the boundaries, provided that the initial condition is strictly positive [22].  
 451 In this case, the existence of  $m$  as assumed in Theorem 5.2 is then guaranteed by  
 452  $z^* \in \mathbb{R}_{>0}^d$ .

453 *Remark 5.4.* Theorem 5.2 implies finite dimensional distribution convergence of  
 454  $Y^V$  to  $Y$  in the following sense: for all  $0 \leq t_1 < t_2 < \dots < t_n \leq T$  we have

$$455 \quad P\left(\max_{1 \leq i \leq n} \|Y^V(t_i) - Y(t_i)\|_\infty > 0\right) \leq \sum_{i=1}^n P(\|Y^V(t_i) - Y(t_i)\|_\infty > 0),$$

456 and the latter tends to 0 as  $V$  tends to  $\infty$ , under the conditions of Theorem 5.2.

457 Some simulations of the process  $Y$  are proposed in Figure 2 for the case of the  
 458 SIS model (4.2). We conclude this section with the following result, concerning the  
 459 convergence of  $Y^V$  to  $Y$  as processes with sample paths in  $D_{\tilde{\mathcal{X}}}[0, T]$ . We note how  
 460 this result is necessary for the convergence of continuous functionals of  $D_{\tilde{\mathcal{X}}}[0, T]$ , as  
 461 highlighted in Section 5.2.

462 **THEOREM 5.5.** *Assume that Assumption 3.1 holds. Furthermore, assume that the*  
 463 *random variables  $X^V(0)/V$  converge weakly to a constant  $z^*$  as  $V$  goes to infinity,*  
 464 *and let  $Z(0) = z^*$ . Assume that the solution  $Z$  to (2.2) with  $Z(0) = z^*$  exists over*  
 465 *the interval  $[0, T]$  and that*

$$466 \quad m = \min_{\substack{S \in \tilde{\mathcal{X}} \\ u \in [0, T]}} Z_S(u) > 0.$$

467 Finally, assume that  $Y^V(0) = Y(0)$  for all positive integers  $V$ . Then  $Y^V$  converges  
 468 in probability to  $Y$  as processes with sample paths in  $D_{\tilde{\mathcal{X}}}[0, T]$  (where we identify  $\tilde{\mathcal{X}}$   
 469 with the elements of the canonical basis of  $\mathbb{R}^{|\tilde{\mathcal{X}}|}$  and embed it with the metric  $\|\cdot\|_\infty$ ,  
 470 or any equivalent one).

471 The proof is given in Appendix A.

472 **5.2. Applications of Theorem 5.5.** The convergence of Theorem 5.5 allows  
 473 us to state convergence in probability of  $f(Y^V)$  to  $f(Y)$ , where  $f: D_{\tilde{\mathcal{X}}}[0, T] \rightarrow \mathbb{R}$  is  
 474 a functional that is continuous with respect to the Skorohod  $J_1$  topology. Classical  
 475 examples are  $f(x) = \sup_{t \in [0, T]} \|x(t)\|_\infty$ ,  $f(x) = \int_0^T \phi(x(s)) ds$  for some continuous  
 476 function  $\phi$ , or  $f(x) = \sup_{t \in [0, T]} (x(t) - x(t-))$  where  $x(t-) = \lim_{h \uparrow t} x(h)$  (see for  
 477 example [11, Chapter 3]). More concretely, a functional we may want to consider is  
 478 the number of times an individual gets infected in the interval  $[0, T]$ , assuming the  
 479 model of equation (4.2) is in place. We denote this functional by  $\psi$ . Note that the  
 480 convergence of  $X^V/V$  to its deterministic fluid limit, as stated in Theorem 3.2, does  
 481 not give any mean of inferring the distribution of  $\psi(Y^V)$ . However, knowing that

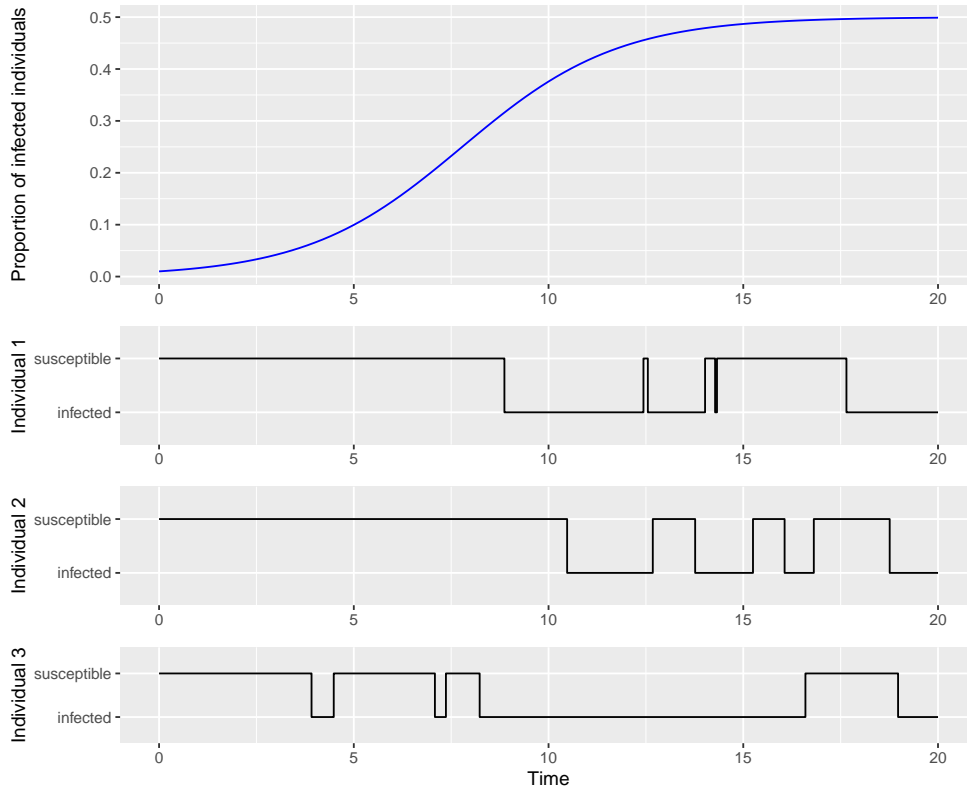
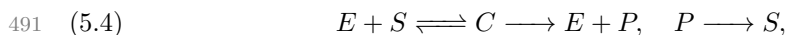


FIG. 2. *The process  $Y$  in SIS model.* Consider the model (4.2), and let  $Y$  be as in (5.2). The first panel shows the concentration of infected individuals  $Z_I$  according to the deterministic solution to (2.2) with  $Z_S(0) = 0.99$  and  $Z_I(0) = 0.01$ . Mass-action kinetics is assumed, with the rate constants of  $S + I \rightarrow 2I$  and  $I \rightarrow S$  being 1 and 0.5, respectively. According to (5.2),  $Z_I$  determines the rate at which the single-individual process  $Y$  turns from 'susceptible' to 'infected'. The last three panels show independent realizations of  $Y$ . The times in the x-axes of the four panels are aligned.

482  $\psi(Y^V)$  converges in probability to  $\psi(Y)$ , if  $V$  is large enough we can approximate the  
 483 distribution of the former by the distribution of the latter. Obtaining an estimate of  
 484 the distribution of  $\psi(Y)$  only requires the simulation of enough independent copies of  
 485  $Y$ , whose jump rates are deterministic and therefore do not require a simulation of  
 486  $X^V$  to be computed, as opposed to the much more expensive strategy of simulating  
 487 multiple independent trajectories of  $(Y^V, X^V)$  via the Gillespie algorithm (which is  
 488 especially cumbersome for large values of  $V$ ). The empirical distributions obtained  
 489 with the two strategies are compared in Figure 3. Similarly, we can apply our results  
 490 to a Michaelis-Menten mechanism. Consider the model



492 where the enzyme activities counterbalances a spontaneous transformation of mole-  
 493 cules of type  $P$  into molecules of type  $S$ . To measure the activity level of the enzymes,  
 494 we may want to study for how long a randomly chosen enzyme molecule is in bound  
 495 state  $C$  up to a given time  $T$ . Let us call this quantity  $\nu(Y^V)$ . The classical scal-

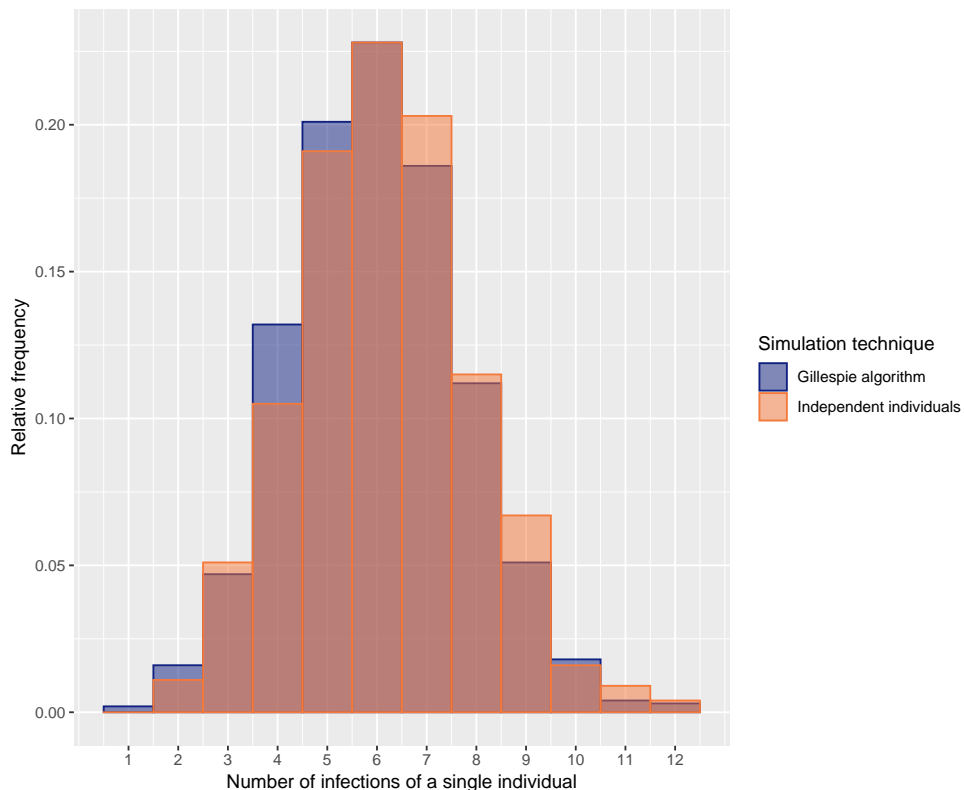


FIG. 3. **Empirical distribution of number of infections in SIS model.** Consider the model (4.2), and let  $\psi$  be the number of infections a randomly selected individual undergoes up to time  $T$ . The empirical distributions of  $\psi(Y^V)$  and  $\psi(Y)$  are compared, the former obtained by the simulation of 1,000 independent copies of  $(Y^V, X^V)$  via the Gillespie algorithm (applied to the formulation in terms of usual stochastic reaction networks discussed in Section 4.1), and the latter obtained via the simulation of 1,000 copies of  $Y$ . Here,  $V = 1,000$  and the initial portion of infected individuals is 1% (so we are initially close to the boundary and we may expect some minor discrepancy between  $X^V/V$  and its deterministic limit  $Z$ , see also Figure 5). Mass-action kinetics is assumed, with the rate constants of  $S + I \rightarrow 2I$  and  $I \rightarrow S$  being 1 and 0.5, respectively.

496 ing of Theorem 3.2 does not allow for inference of the distribution of  $v(Y^V)$ , but  
 497 Theorem 5.5 ensures that it converges to the distribution of  $v(Y)$  as  $V$  tends to  $\infty$ .  
 498 Figure 4 compares the empirical distributions of  $v(Y^V)$  and  $v(Y)$  obtained by the  
 499 simulation of 1,000 independent copies of  $(Y^V, X^V)$  and 1,000 independent copies of  
 500  $Y$ , respectively. For this comparison we chose  $V = 1,000$ .

501 **5.3. Approximating the system dynamics with single-molecule trajec-**  
 502 **tories.** Let  $\bar{\mathcal{X}} \subseteq \mathcal{X}$  be the set of species that can be tracked in some form:

$$503 \quad \bar{\mathcal{X}} = \{S \in \mathcal{X} : S = \tau(\tilde{S}) \text{ for some } \tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}\}.$$

504 Moreover, let  $\pi: \mathbb{R}^d \rightarrow \mathbb{R}^{|\bar{\mathcal{X}}|}$  be the projection of the state space onto the coordinates  
 505 relative to the species in  $\bar{\mathcal{X}}$ . The aim of this section is to approximate the dynamics  
 506 of  $\pi(X^V)$  by means of a sum of *independent* processes distributed as in (5.2) (po-  
 507 tentially with rescaled dynamics, as shown in the statement of Theorem 5.8). Note

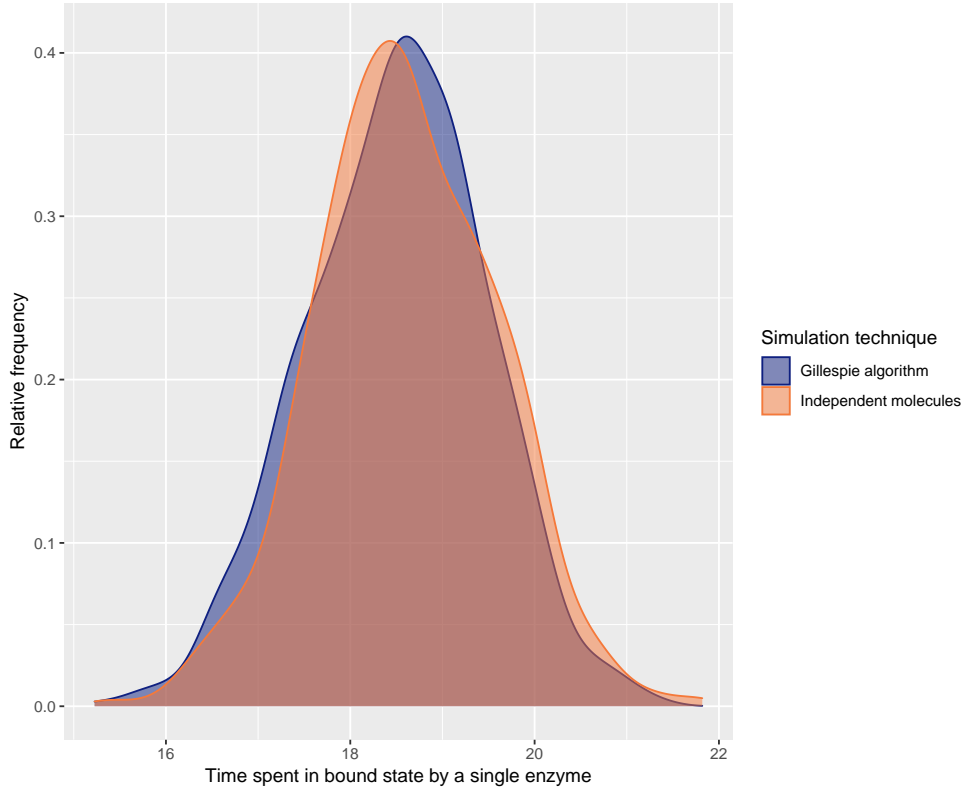


FIG. 4. **Empirical density of time in bound state in Michaelis-Menten model.** Consider the model (5.4), and let  $v$  be the time a randomly selected molecule of enzyme is in bound state  $C$  up to time  $T$ . The empirical distributions of  $v(Y^V)$  and  $v(Y)$  are compared, the former obtained by the simulation of 1,000 independent copies of  $(Y^V, X^V)$  via the Gillespie algorithm (applied to the formulation in terms of usual stochastic reaction networks discussed in Section 4.1), and the latter obtained via the simulation of 1,000 copies of  $Y$ . Here,  $V = 1,000$  and  $Z(0) = X(0)/V = (0.5, 10, 0.5, 1)$ , where the species are ordered as in  $E, S, C, P$ . Mass-action kinetics is assumed, with the rate constants of  $E + S \rightarrow C$ ,  $C \rightarrow E + S$ ,  $C \rightarrow E + P$ , and  $P \rightarrow S$  being 1, 5, 1, and 0.5, respectively.

508 that the goal of such an approximation is not to provide a faster simulation method  
 509 than those present in the literature: our goal is to break down the dynamics of sev-  
 510 eral correlated particles into a set of independent single-molecule trajectories which  
 511 could be simulated simultaneously by a highly parallelizable algorithm. We begin by  
 512 identifying each trackable species  $\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}$  with a different physical portions of  
 513 the chemical species  $\tau(\tilde{S})$ :  $m$  molecules of species  $S \in \mathcal{X}$  are available at time  $t$  if and  
 514 only if the quantity of each trackable species  $\tilde{S}$  satisfying  $\tau(\tilde{S}) = S$  is  $m$  at time  $t$ .  
 515 Under this assumption, clearly the process  $X^V$  can be expressed in terms of the dy-  
 516 namics of its individual trackable species, which are typically not independent of each  
 517 other. We further restrict ourselves to models that are *sub-conservative* with respect  
 518 to the trackable species. This means that while trackable species can potentially be  
 519 degraded (by entering the fictitious state  $\Delta$ ), their total mass never increases. Equiv-  
 520 alently, we assume that each time a trackable species is created it is by transformation

521 of another trackable species. We assume sub-conservativeness because we want the  
 522 single-molecule fates we track to be independent, while their agglomeration is still  
 523 able to approximately describe the dynamics of the whole system. If we allowed for  
 524 mass creation, we would need to introduce new molecules over time and track them.  
 525 Defining the molecule creation times over a finite interval of time independently on  
 526 each other is technically possible if the creation rate is deterministic: it is sufficient to  
 527 first simulate a Poisson random variable counting the total number of new molecules  
 528 in the finite time interval, then consider each creation time as independent on the  
 529 others with probability density proportional to the deterministic creation rate. How-  
 530 ever, this procedure requires the introduction of further notation and for the sake of  
 531 clarity we decided to only present the simpler case of sub-conservative models (with  
 532 respect to the trackable species).

533 *Assumption 5.6.* Let  $(Y^V, X^V)$  be a family of stochastic reaction systems with  
 534 trackable species. We assume that for each reaction  $y \rightarrow y' \in \mathcal{R}$  and for each  $\tilde{S}' \in$   
 535  $\tilde{\mathcal{X}} \setminus \{\Delta\}$

$$536 \quad \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') = y'_{\tau(\tilde{S}'')}$$

537 For all  $S \in \bar{\mathcal{X}}, \tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}$  define

$$538 \quad \tau^{-1}(S) = \{\tilde{S}' \in \tilde{\mathcal{X}} : \tau(\tilde{S}') = S\} \quad \text{and} \quad \alpha(S) = \#\tau^{-1}(S)$$

539 The sub-conservation of the model with respect to the trackable species is formally  
 540 stated as follows.

541 *LEMMA 5.7.* *Let  $(Y^V, X^V)$  be a family of stochastic reaction systems with track-*  
 542 *able species satisfying Assumption 5.6. Then, for all  $V \in \mathbb{Z}_{\geq 1}$  and for all  $t \in \mathbb{R}_{>0}$*

$$543 \quad (5.5) \quad \|\pi(X^V(t))\|_1 \leq \sum_{S \in \bar{\mathcal{X}}} \alpha(S) X_S^V(t) \leq \sum_{S \in \bar{\mathcal{X}}} \alpha(S) X_S^V(0).$$

544 *Proof.* The first inequality of (5.5) simply follows from the fact that the quantities  
 545  $\alpha(S)$  are greater than or equal to 1. For the second inequality, simply note that if a  
 546 reaction  $y \rightarrow y' \in \mathcal{R}$  occurs at time  $t$ , then

$$\begin{aligned} 547 \quad \sum_{S \in \bar{\mathcal{X}}} \alpha(S) X_S^V(t) - \sum_{S \in \bar{\mathcal{X}}} \alpha(S) X_S^V(t-) &= \sum_{S \in \bar{\mathcal{X}}} \alpha(S) y'_S - \sum_{S \in \bar{\mathcal{X}}} \alpha(S) y_S \\ 548 \quad &= \sum_{\tilde{S}' \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y'_{\tau(\tilde{S}')} - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} \\ 549 \quad &= \sum_{\tilde{S}' \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} \\ 550 \quad &\leq \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})} = 0. \\ 551 \end{aligned}$$

552 Note that in the third equality we used Assumption 5.6, and in the last equality we  
 553 used  $\sum_{\tilde{S}' \in \tilde{\mathcal{X}} \setminus \{\Delta\}} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \leq 1$ . Since the quantity  $\sum_{S \in \bar{\mathcal{X}}} \alpha(S) X_S^V$  is not increasing  
 554 with the occurrence of a reaction, (5.5) is proven.  $\square$

555 The main result of this section is the following one, a more detailed version of  
 556 which is proven in the Appendix. In particular, in Theorem A.5 a convergence rate  
 557 of the order of  $e^{-C\sqrt{V}}$  for a positive constant  $C$  is proven, provided that the initial  
 558 conditions of  $X^V$  and  $\tilde{X}^V$  are close enough.

559 **THEOREM 5.8.** *Assume that Assumptions 3.1 and 5.6 are satisfied, and consider*  
 560 *a family of stochastic reaction systems with trackable species  $(Y^V, X^V)$ . Assume that*  
 561  *$V^{-1}X^V(0)$  converges in distribution to some  $z^* \in \mathbb{R}_{>0}^d$  as  $V$  goes to infinity and*  
 562  *$E[\pi(X^V(0))] < \infty$  for all  $V \in \mathbb{Z}_{\geq 1}$ . Let  $\tilde{X}^V(0) = \lfloor Vz^* \rfloor$  and define the process  $\tilde{X}^V$*   
 563 *by*

$$564 \quad (5.6) \quad \tilde{X}^V(t) = \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \frac{\tau(Y^{\tilde{S},i}(t))}{\alpha(\tau(Y^{\tilde{S},i}(t)))},$$

565 where the processes  $(Y^{\tilde{S},i})_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}, i \in \mathbb{Z}_{\geq 1}}$  are independent and satisfy

$$566 \quad Y^{\tilde{S},i}(t) = \tilde{S} + \sum_{\tilde{S}''+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} (\tilde{S}'' - \tilde{S}') N_{\tilde{S}''+y \rightarrow \tilde{S}''+y'}^{\tilde{S},i} \left( \int_0^t \lambda_{\tilde{S}''+y \rightarrow \tilde{S}''+y'}(Y^{\tilde{S},i}(u), Z(u)) du \right),$$

567 for a family of independent, identically distributed unit-rate Poisson processes  $\{N_r^{\tilde{S},i}\}_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}, i \in \mathbb{Z}_{\geq 1}, r \in \tilde{\mathcal{R}}}$ .  
 568 Then,

$$569 \quad \lim_{V \rightarrow \infty} E \left[ \sup_{0 \leq s \leq t} \left\| \frac{\pi(X^V(t))}{V} - \frac{\tilde{X}^V(t)}{V} \right\| \right] = 0.$$

570 Note that in the definition of  $\tilde{X}^V$  above we consider as many independent single-  
 571 molecule trajectories as many trackable molecules are in the system at time 0. A  
 572 natural question is whether a good approximation of the original model  $X^V$  can be  
 573 obtained by considering the agglomeration of less independent single-molecule trajec-  
 574 tories. However, a detailed study of the error in this case is out of the scope of the  
 575 present paper.

576 *Example 5.9.* Consider the SIS model of equation (4.2). We assume  $X_S^V(0) =$   
 577  $0.99V$  and  $X_I^V(0) = 0.01V$ , and let  $V = 1,000$ . We wish to approximate the number  
 578 of susceptible individuals by

$$579 \quad \frac{X_S^V(t)}{V} \approx \frac{\tilde{X}_S^V(t)}{V}.$$

580 In order to test the performance of the above approximation, we simulate 100 in-  
 581 dependent copies of  $X^V$  and  $\tilde{X}$ , and plot them against each other in Figure 5. It  
 582 is perhaps not surprising to note a higher variance for the trajectories of  $X^V$  with  
 583 respect of those of  $\tilde{X}^V$ : the former is the result of several single-molecule trajec-  
 584 tories that are naturally correlated with each other, specifically the rate at which a  
 585 single molecule changes state is stochastic and given by the current state of all the  
 586 other molecules. In the approximation, the dynamics of the single tracked molecules  
 587 are independent and their rate of change from one state to another state are purely  
 588 deterministic, which leads to fewer stochastic fluctuations. However, we do observe a  
 589 discrepancy between the two models only at the beginning of the trajectories, when

590 the number of infected individuals is rather low (only 10 individuals in the initial con-  
 591 dition) and the deterministic approximation given by Theorem 3.2 is perhaps not yet  
 592 accurate enough. As a matter of fact, Figure 6 shows that the difference in variance  
 593 is considerably reduced if the initial counts of infected individuals is increased to 100.  
 594

595 We are interested in bounding

$$596 \quad (5.7) \quad P \left( \sup_{0 \leq t \leq T} \left| \frac{X_S^V(t)}{V} - \frac{\tilde{X}_S^V(t)}{V} \right| > \varepsilon \right),$$

597 for a fixed  $\varepsilon \in \mathbb{R}_{>0}$ . Assume mass-action kinetics and let  $\kappa_1$  and  $\kappa_2$  be the rate  
 598 constants of  $S + I \rightarrow 2I$  and  $I \rightarrow S$ , respectively. Moreover, assume for simplicity  
 599 that  $X^V(0) = \tilde{X}^V(0) = VZ(0)$  and  $X_S^V(0) + X_I^V(0) = V$ . Since the total number  
 600 of individual is conserved, for all  $0 \leq t \leq T$  we have  $X_S^V(t) + X_I^V(t) = V$ . By  
 601 superposition there exist two independent unit-rate Poisson processes  $\tilde{N}_{S+I \rightarrow 2I}$  and  
 602  $\tilde{N}_{I \rightarrow S}$  such that for all  $0 \leq t \leq T$  and for a fixed  $V$  we have (with a simplified notation  
 603 that does not take into account the initial values of the independent single individual

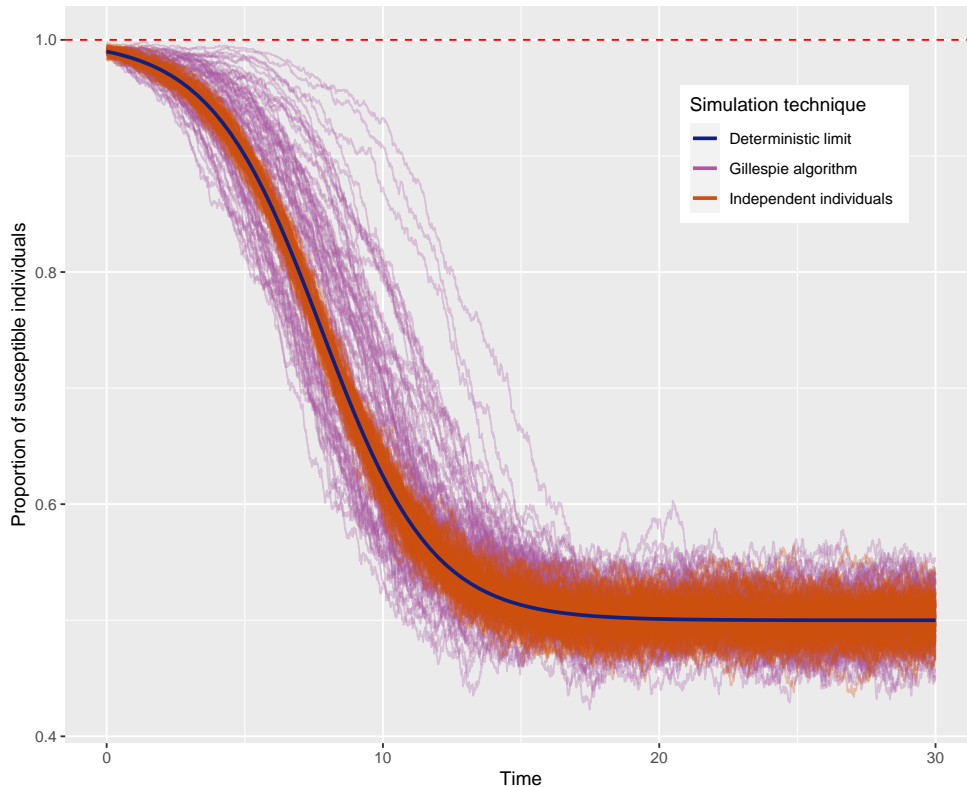


FIG. 5. *Comparison in SIS model.* Comparison of 100 independent trajectories of  $X_S^V/V$  and  $\tilde{X}_S^V/V$ , considering the SIS model described in (4.2). Here,  $X_S^V(0) = 0.99V$ ,  $X_I^V(0) = 0.01V$ , and  $V = 1,000$ . Mass-action kinetics is assumed, with the rate constants of  $S + I \rightarrow 2I$  and  $I \rightarrow S$  being 1 and 0.5, respectively.

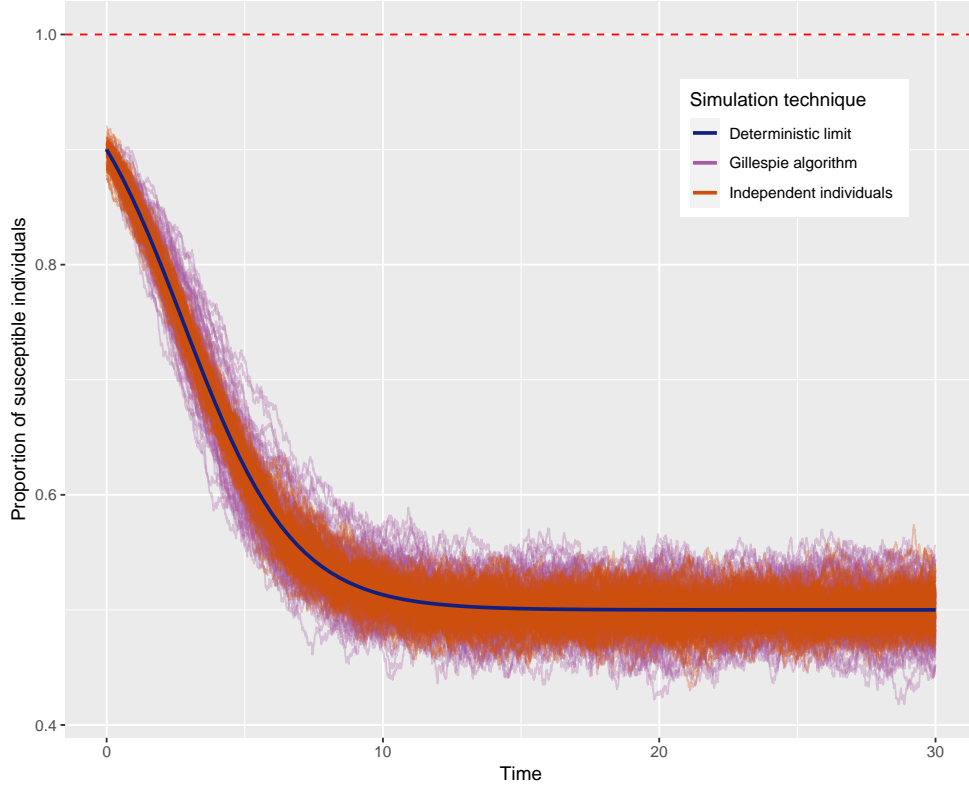


FIG. 6. **Comparison in SIS model.** Comparison of 100 independent trajectories of  $X_S^V/V$  and  $\tilde{X}_S^V/V$ , considering the SIS model described in (4.2). Here,  $X_S^V(0) = 0.9V$ ,  $X_I^V(0) = 0.1V$ , and  $V = 1,000$ . Mass-action kinetics is assumed, with the rate constants of  $S + I \rightarrow 2I$  and  $I \rightarrow S$  being 1 and 0.5, respectively.

604 trajectories)

$$605 \quad \tilde{N}_{S+I \rightarrow 2I} \left( \int_0^t \kappa_1 \tilde{X}_S^V(u) Z_I(u) du \right) = \sum_{i=1}^V N_{\tilde{S}+S+I \rightarrow \tilde{I}+2I}^i \left( \int_0^t \mathbb{1}_{\{\tilde{S}\}}(Y^i(u)) Z_I(u) du \right)$$

$$606 \quad \tilde{N}_{I \rightarrow S} \left( \int_0^t \kappa_2 \tilde{X}_I^V(u) du \right) = \sum_{i=1}^V N_{\tilde{I}+I \rightarrow \tilde{S}+S}^i \left( \int_0^t \mathbb{1}_{\{\tilde{I}\}}(Y^i(u)) du \right).$$

607

608 Then,

$$609 \quad \left| \frac{X_S^V(t)}{V} - \frac{\tilde{X}_S^V(t)}{V} \right| \leq \Delta(t) + \frac{1}{V} \int_0^t \kappa_1 X_S^V(u) \left| \frac{X_I^V(u)}{V} - Z_I(u) \right| du$$

$$610 \quad + \int_0^t \kappa_1 \left| \frac{X_S^V(u)}{V} - \frac{\tilde{X}_S^V(u)}{V} \right| Z_I(u) du + \int_0^t \kappa_2 \left| \frac{X_I^V(u)}{V} - \frac{\tilde{X}_I^V(u)}{V} \right| du,$$

611

612

613 where

$$\begin{aligned}
614 \quad \Delta(t) &= \frac{1}{V} \left| N_{S+I \rightarrow 2I} \left( \int_0^t \frac{\kappa_1}{V} X_S^V(u) X_I^V(u) du \right) - \int_0^t \frac{\kappa_1}{V} X_S^V(u) X_I^V(u) du \right| \\
615 &\quad + \frac{1}{V} \left| N_{I \rightarrow S} \left( \int_0^t \kappa_2 X_I^V(u) du \right) - \int_0^t \kappa_2 X_I^V(u) du \right| \\
616 &\quad + \frac{1}{V} \left| \tilde{N}_{S+I \rightarrow 2I} \left( \int_0^t \kappa_1 \tilde{X}_S^V(u) Z_I(u) du \right) - \int_0^t \kappa_1 \tilde{X}_S^V(u) Z_I(u) du \right| \\
617 &\quad + \frac{1}{V} \left| \tilde{N}_{I \rightarrow S} \left( \int_0^t \kappa_2 \tilde{X}_I^V(u) du \right) - \int_0^t \kappa_2 \tilde{X}_I^V(u) du \right|.
\end{aligned}$$

619 Using  $X_I^V(t) = V - X_S^V(t)$  and  $Z_I(t) \leq 1$  for all  $0 \leq t \leq T$  we obtain

$$\begin{aligned}
620 \quad \left| \frac{X_S^V(t)}{V} - \frac{\tilde{X}_S^V(t)}{V} \right| &\leq \Delta(t) + \int_0^t \kappa_1 \left| \frac{X_I^V(u)}{V} - Z_I(u) \right| du \\
621 &\quad + \int_0^t (\kappa_1 + \kappa_2) \left| \frac{X_S^V(u)}{V} - \frac{\tilde{X}_S^V(u)}{V} \right| du.
\end{aligned}$$

624 By taking the supremum on  $0 \leq t \leq T$  on both sides and by applying the Gronwall inequality, we have

$$626 \quad \sup_{0 \leq t \leq T} \left| \frac{X_S^V(t)}{V} - \frac{\tilde{X}_S^V(t)}{V} \right| \leq \left( \sup_{0 \leq t \leq T} \Delta(t) + \kappa_1 T \sup_{0 \leq t \leq T} \left| \frac{X_I^V(u)}{V} - Z_I(u) \right| \right) e^{(\kappa_1 + \kappa_2)T}.$$

627 For notational convenience, let  $\nu = \varepsilon e^{-(\kappa_1 + \kappa_2)T}$ . Hence, (5.7) is smaller than

$$628 \quad (5.8) \quad P \left( \sup_{0 \leq t \leq T} \Delta(t) > \frac{\nu}{2} \right) + P \left( \sup_{0 \leq t \leq T} \left| \frac{X_I^V(u)}{V} - Z_I(u) \right| > \frac{\nu}{2\kappa_1 T} \right).$$

629 By noting that  $P(\sup_{0 \leq t \leq T} \Delta(t) > \nu/2)$  is smaller than

$$\begin{aligned}
630 \quad &P \left( \sup_{0 \leq t \leq T} \frac{1}{V} \left| N_{S+I \rightarrow 2I} \left( \int_0^t \frac{\kappa_1}{V} X_S^V(u) X_I^V(u) du \right) - \int_0^t \frac{\kappa_1}{V} X_S^V(u) X_I^V(u) du \right| > \frac{\nu}{8} \right) \\
631 &+ P \left( \sup_{0 \leq t \leq T} \frac{1}{V} \left| N_{I \rightarrow S} \left( \int_0^t \kappa_2 X_I^V(u) du \right) - \int_0^t \kappa_2 X_I^V(u) du \right| > \frac{\nu}{8} \right) \\
632 &+ P \left( \sup_{0 \leq t \leq T} \frac{1}{V} \left| \tilde{N}_{S+I \rightarrow 2I} \left( \int_0^t \kappa_1 \tilde{X}_S^V(u) Z_I(u) du \right) - \int_0^t \kappa_1 \tilde{X}_S^V(u) Z_I(u) du \right| > \frac{\nu}{8} \right) \\
633 &+ P \left( \sup_{0 \leq t \leq T} \frac{1}{V} \left| \tilde{N}_{I \rightarrow S} \left( \int_0^t \kappa_2 \tilde{X}_I^V(u) du \right) - \int_0^t \kappa_2 \tilde{X}_I^V(u) du \right| > \frac{\nu}{8} \right),
\end{aligned}$$

635 we obtain that (5.8) is smaller than

$$\begin{aligned}
636 & \\
637 \quad &12 \exp \left( \frac{\kappa_1 \varepsilon T}{2} - \frac{\nu}{24} \sqrt{V} \right) + 12 \exp \left( \frac{\kappa_2 \varepsilon T}{2} - \frac{\nu}{24} \sqrt{V} \right) \\
638 &+ 6 \exp \left( \frac{\kappa_1 \varepsilon T}{2} \left( 1 + \frac{\nu}{\kappa_1 T} \right)^2 + \frac{\kappa_2 \varepsilon T}{2} \left( 1 + \frac{\nu}{\kappa_1 T} \right) - \frac{\nu}{12\kappa_1 T} e^{-T(\kappa_1 - \kappa_2) - \nu} \sqrt{V} \right) \\
639 &
\end{aligned}$$

640 by Lemma A.1 and Theorem A.2 (for the special case of the SIS model, see Exam-  
 641 ple A.3). We note that  $\exp(h)$  is defined as  $e^h$  for all real numbers  $h$ . It follows  
 642 that (5.7) tends to 0 as  $V$  tends to  $\infty$  with the same rate as  $e^{-C\sqrt{V}}$  for some positive  
 643 constant  $C$ . This is always the case, and bounds for more general models are provided  
 644 by Theorem A.5.

### 645 Appendix A. Proofs and explicit bounds.

646 In this section we give proofs for the results stated above, together with more  
 647 precise bounds on the quantities of interest. To this aim, we first define the following  
 648 quantities: for all  $V \in \mathbb{Z}_{\geq 1}$  and  $\varepsilon \in \mathbb{R}_{>0}$  let

$$649 \mathcal{A}_{V,\varepsilon,t} = \left\{ \sup_{u \in [0,t]} \left\| \frac{X^V(u)}{V} - Z(u) \right\|_{\infty} \leq \varepsilon \right\} \quad \text{and} \quad p^{V,\varepsilon,t} = P(\mathcal{A}_{V,\varepsilon,t}^c) = 1 - P(\mathcal{A}_{V,\varepsilon,t}),$$

650 where the superscript ‘‘c’’ denotes the complement. Note that, for any fixed  $V$  and  $\varepsilon$ ,  
 651 the sequence of events  $\mathcal{A}_{V,\varepsilon,t}$  is monotone in  $t$ , and  $p^{V,\varepsilon,t}$  is a non-decreasing  
 652 function of  $t$  attaining its maximum for the value  $t = T$ .

653 Define the  $\mathbb{Z}_{\geq 0}^d$ -valued process  $X^{V,\varepsilon}$  on  $[0, T]$  in the following way: for any  $S \in \mathcal{X}$   
 654 and any  $t \in [0, T]$ , let

$$655 (A.1) \quad X_S^{V,\varepsilon}(t) = \min\{\max\{X_S^V(t), VZ_S(t) - V\varepsilon\}, VZ_S(t) + V\varepsilon\}.$$

656 Hence, by definition for all  $t \in \mathbb{R}_{>0}$

$$657 \left\| \frac{X^{V,\varepsilon}(t)}{V} - Z(t) \right\|_{\infty} \leq \varepsilon.$$

658 Moreover, define the process  $\hat{X}^{V,\varepsilon}$  by

$$659 \hat{X}^{V,\varepsilon}(t) = X^V(0) + \sum_{y \rightarrow y' \in \mathcal{R}} (y' - y) N_{y \rightarrow y'} \left( \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \right)$$

660 for all  $t \in [0, T]$ , where the processes  $N_{y \rightarrow y'}$  are the same as in (4.6). Note that for  
 661 any  $t \in [0, T]$  we have  $\mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}} X^{V,\varepsilon}(t) = \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}} X^V(t) = \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}} \hat{X}^{V,\varepsilon}(t)$ . In particular,  
 662 it follows that

$$663 \sup_{0 \leq u \leq t} \left\| \frac{X^{V,\varepsilon}(u)}{V} - Z(u) \right\|_{\infty} \leq \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}} \sup_{0 \leq u \leq t} \left\| \frac{\hat{X}^{V,\varepsilon}(u)}{V} - Z(u) \right\|_{\infty} + \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}^c} \varepsilon$$

$$664 (A.2) \quad \leq \sup_{0 \leq u \leq t} \left\| \frac{\hat{X}^{V,\varepsilon}(u)}{V} - Z(u) \right\|_{\infty}.$$

666 For any  $t \in [0, T]$  and any  $\varepsilon \in \mathbb{R}_{>0}$  let

$$667 \Omega_1^{\varepsilon,t} = \{Z(u) + h : u \in [0, t], h \in \mathbb{R}^d, \|h\|_{\infty} \leq \varepsilon\} \cap \mathbb{R}_{\geq 0}^d$$

668 be the (one-dimensional) neighbourhood of the solution  $Z$  on the interval  $[0, t]$  with  
 669 amplitude  $\varepsilon$ , intersected with the non-negative orthant. Note that for all  $t \in [0, T]$  we  
 670 have  $X^{V,\varepsilon}(t)/V \in \Omega_1^{\varepsilon,V}$ . Similarly, let

$$671 \Omega_2^{\varepsilon,t} = \{(Z(u) + h, Z(u) + h') : u \in [0, t], h, h' \in \mathbb{R}^d, \|h\|_{\infty} \leq \varepsilon, \|h'\|_{\infty} \leq \varepsilon\} \cap \mathbb{R}_{\geq 0}^{2d}$$

672 be the two-dimensional neighbourhood of the  $Z$  restricted to  $[0, t]$  with amplitude  $\varepsilon$ ,  
 673 intersected with the non-negative orthant.

674 To conclude, it is convenient to introduce in this section a notation for centered  
 675 Poisson processes: given a Poisson process  $N$ , we denote by  $\bar{N}$  the process defined  
 676 by  $\bar{N}(t) = N(t) - t$  for all  $t \in \mathbb{R}_{\geq 0}$ . In order to bound  $p^{V, \varepsilon, t}$  from above and prove  
 677 Theorem 5.8 we need the following results concerning centered Poisson processes. For  
 678 completeness, we provide a proof as we were not able to find it in the literature, even  
 679 if small variations of Lemma A.1 are well-known and obtained as an application of  
 680 Doob's inequality or Kolmogorov's maximal inequality.

681 LEMMA A.1. *Let  $N$  be a Poisson process and let  $T, \varepsilon \in \mathbb{R}_{>0}$ . Then, for all  $n \in$   
 682  $\mathbb{Z}_{\geq 1}$*

$$683 \quad P \left( \sup_{t \in [0, nT]} \left| \frac{\bar{N}(t)}{n} \right| > \varepsilon \right) \leq 6 \exp \left( \frac{e}{2} T - \frac{\varepsilon \sqrt{n}}{3} \right).$$

684 *Proof.* For all  $j \in \mathbb{Z}_{\geq 1}$  and all  $h \in \mathbb{R}_{>0}$  define

$$685 \quad (\text{A.3}) \quad \Xi_j^h = \bigcup_{i=0}^{2^j h} \left\{ \frac{i}{2^j} \right\}.$$

686 Since  $\bar{N}$  is almost surely right continuous, we have that for all  $n \in \mathbb{Z}_{\geq 1}$  and all  
 687  $T \in \mathbb{R}_{>0}$

$$688 \quad \sup_{t \in [0, nT]} \left| \frac{\bar{N}(t)}{n} \right| = \lim_{j \rightarrow \infty} \max_{t \in \Xi_j^{nT}} \left| \frac{\bar{N}(t)}{n} \right|$$

689 almost surely. Since for all  $j \in \mathbb{Z}_{\geq 1}$  we have  $\Xi_j^{nT} \subset \Xi_{j+1}^{nT}$ , by continuity of the  
 690 probability measure we have

$$691 \quad P \left( \sup_{t \in [0, nT]} \left| \frac{\bar{N}(t)}{n} \right| > \varepsilon \right) = \lim_{j \rightarrow \infty} P \left( \max_{t \in \Xi_j^{nT}} \left| \frac{\bar{N}(t)}{n} \right| > \varepsilon \right).$$

692 By Etemadi's inequality we have

$$693 \quad P \left( \max_{t \in \Xi_j^{nT}} \left| \frac{\bar{N}(t)}{n} \right| > \varepsilon \right) \leq 3 \max_{t \in \Xi_j^{nT}} P \left( \left| \frac{\bar{N}(t)}{n} \right| > \frac{\varepsilon}{3} \right).$$

694 Moreover, for any real  $\beta \in (0, 1)$  and any real  $t \in (0, nT)$  we have

$$\begin{aligned} 695 \quad P \left( \left| \frac{\bar{N}(t)}{n} \right| > \frac{\varepsilon}{3} \right) &\leq P \left( \frac{\bar{N}(t)}{n} > \frac{\varepsilon}{3} \right) + P \left( -\frac{\bar{N}(t)}{n} > \frac{\varepsilon}{3} \right) \\ 696 \quad &= P \left( e^{\frac{n^\beta \bar{N}(t)}{n}} > e^{\frac{n^\beta \varepsilon}{3}} \right) + P \left( e^{-\frac{n^\beta \bar{N}(t)}{n}} > e^{\frac{n^\beta \varepsilon}{3}} \right) \\ 697 \quad &\leq 2 \exp \left( -\frac{n^\beta \varepsilon}{3} \right) \exp \left( t(e^{n^{\beta-1}} - 1 - n^{\beta-1}) \right) \\ 698 \quad &\leq 2 \exp \left( -\frac{n^\beta \varepsilon}{3} \right) \exp \left( nT \frac{n^{2\beta-2}}{2} e^{n^{\beta-1}} \right), \\ 699 \quad &\leq 2 \exp \left( -\frac{n^\beta \varepsilon}{3} \right) \exp \left( nT \frac{n^{2\beta-2}}{2} e \right), \\ 700 \end{aligned}$$

701 where the inequality in the third line follows from the Markov's inequality and the  
 702 known form of the moment generating function of a Poisson random variable, which  
 703 leads to  $E[e^{n^{\beta-1}\bar{N}(t)}] = e^{-n^{\beta-1}t}e^{t(e^{n^{\beta-1}}-1)}$  and  $E[e^{-n^{\beta-1}\bar{N}(t)}] = e^{n^{\beta-1}t}e^{t(e^{-n^{\beta-1}}-1)}$ .  
 704 Hence, for all  $n \in \mathbb{Z}_{\geq 1}$  we have that both  $E[e^{n^{\beta-1}\bar{N}(t)}]$  and  $E[e^{-n^{\beta-1}\bar{N}(t)}]$  are less than  
 705 or equal to  $e^{t(e^{n^{\beta-1}}-1-n^{\beta-1})}$ . The inequality in the fourth line derives from the Taylor  
 706 expansion of the exponential function. By choosing  $\beta = 1/2$  we have

$$707 \quad P\left(\left|\frac{\bar{N}(t)}{n}\right| > \frac{\varepsilon}{3}\right) \leq 2 \exp\left(-\frac{\varepsilon\sqrt{n}}{3}\right) \exp\left(\frac{e}{2}T\right),$$

708 which completes the proof.  $\square$

709 **A.1. Estimates for  $p^{V,\varepsilon,t}$ .** Many papers have focused on quantifying the dis-  
 710 tance between the process  $X^V$  and its fluid limit  $Z$ . Among these, we list [1–3, 13,  
 711 17, 20] with no claim of completeness. Here we use Lemma A.1 to show the following  
 712 upper bound on  $p^{V,\varepsilon,t}$ . While similar estimates are known in the reaction network  
 713 community, we give a formal proof of the bound we propose as we could not find it  
 714 in the literature. Before stating the result, we define the following quantities:

$$715 \quad R = \max_{y \rightarrow y' \in \mathcal{R}} \|y' - y\|_{\infty},$$

$$716 \quad \Lambda_0^{\varepsilon,t} = \sup_{z \in \Omega_1^{\varepsilon,t}} \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(z), \quad \Lambda_1^{\varepsilon,t} = \int_0^t \Lambda_0^{\varepsilon,u} du$$

$$717 \quad L_0^{\varepsilon,t} = \sup_{\substack{(z,z') \in \Omega_2^{\varepsilon,t} \\ z \neq z'}} \sum_{y \rightarrow y' \in \mathcal{R}} \frac{|\lambda_{y \rightarrow y'}(z) - \lambda_{y \rightarrow y'}(z')|}{\|z - z'\|_{\infty}}, \quad L_1^{\varepsilon,t} = \int_0^t L_0^{\varepsilon,u} du$$

$$718 \quad \delta_0^{V,\varepsilon,t} = \sup_{z \in \Omega_1^{\varepsilon,t}} \sum_{y \rightarrow y' \in \mathcal{R}} \left| \frac{\lambda_{y \rightarrow y'}^V(\lfloor Vz \rfloor)}{V} - \lambda_{y \rightarrow y'}(z) \right|, \quad \delta_1^{V,\varepsilon,t} = \int_0^t \delta_0^{V,\varepsilon,u} du$$

$$719 \quad \eta^{V,\varepsilon,t}(\gamma) = e^{-L_1^{2\varepsilon,t}} \gamma \varepsilon - \delta_1^{V,2\varepsilon,t},$$

721 where in the last definition  $\gamma$  is any real number in  $(0, 1]$ . Note that  $\Lambda_0^{\varepsilon,t}$  and  $\delta_0^{V,\varepsilon,t}$  are  
 722 finite for any  $t \in [0, T]$ , since the solution  $Z$  exists up to time  $T$  and the functions  $\lambda_{y \rightarrow y'}$   
 723 are locally Lipschitz by Assumption 3.1. The local Lipschitzianity of the functions  
 724  $\lambda_{y \rightarrow y'}$  also implies that  $L_0^{\varepsilon,t}$  is finite for all  $\varepsilon \in \mathbb{R}_{>0}$  and  $t \in [0, T]$ . It also follows  
 725 from Assumption 3.1 that  $\delta_0^{V,\varepsilon,t}$  tends to zero as  $V$  tends to infinity. Furthermore,  
 726 note that for fixed  $V \in \mathbb{Z}_{\geq 1}$  and  $\varepsilon \in \mathbb{R}_{>0}$ , the quantities  $\Lambda_0^{\varepsilon,t}$ ,  $L_0^{\varepsilon,t}$ , and  $\delta_0^{V,\varepsilon,t}$  are  
 727 all non-decreasing functions of  $t$ . As a consequence, for all  $t \in [0, T]$ ,  $\varepsilon \in \mathbb{R}_{>0}$ , and  
 728  $V \in \mathbb{Z}_{\geq 1}$  we have

$$729 \quad \Lambda_1^{\varepsilon,t} \leq t\Lambda_0^{\varepsilon,t}, \quad L_1^{\varepsilon,t} \leq tL_0^{\varepsilon,t}, \quad \text{and} \quad \delta_1^{V,\varepsilon,t} \leq t\delta_0^{V,\varepsilon,t}.$$

730 It follows that for all  $t \in [0, T]$ ,  $\varepsilon \in \mathbb{R}_{>0}$ , and  $\gamma \in (0, 1]$  the quantity  $\eta^{V,\varepsilon,t}(\gamma)$  tends to  
 731 the positive quantity  $e^{-L_1^{2\varepsilon,t}} \gamma \varepsilon$  as  $V$  tends to infinity. We can now state the following  
 732 theorem.

733 **THEOREM A.2.** *For any  $\varepsilon, t \in \mathbb{R}_{>0}$ , any  $\gamma \in (0, 1]$ , and any  $V \in \mathbb{Z}_{\geq 1}$  large*  
 734 *enough such that  $\eta^{V,2\varepsilon,t}(\gamma) > 0$ , we have*

$$735 \quad p^{V,\varepsilon,t} \leq p^{V,(1-\gamma)\varepsilon e^{-L_1^{2\varepsilon,t}},0} + 6 \exp\left(\frac{e}{2}\Lambda_1^{2\varepsilon,t} + \frac{e}{2}\delta_1^{V,2\varepsilon,t} - \frac{1}{3R}\eta^{V,\varepsilon,t}(\gamma)\sqrt{V}\right)$$

736 *Proof.* First, note that

$$737 \quad p^{V,\varepsilon,t} = P \left( \sup_{u \in [0,t]} \left\| \frac{X^V(u)}{V} - Z(u) \right\|_\infty > \varepsilon \right) = P \left( \sup_{u \in [0,t]} \left\| \frac{X^{V,2\varepsilon}(u)}{V} - Z(u) \right\|_\infty > \varepsilon \right)$$

$$738 \quad = P \left( \sup_{u \in [0,t]} \left\| \frac{\hat{X}^{V,2\varepsilon}(u)}{V} - Z(u) \right\|_\infty > \varepsilon \right).$$

740 Moreover, by superposition, for all  $V \in \mathbb{Z}_{\geq 1}$  and all  $\varepsilon \in \mathbb{R}_{>0}$  we can define a unit-rate  
741 Poisson process  $U^{V,2\varepsilon}$  coupled with  $X^V$  in such a way that for all  $t \in \mathbb{R}_{\geq 0}$

$$742 \quad U^{V,2\varepsilon} \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(u)) du \right) = \sum_{y \rightarrow y' \in \mathcal{R}} N_{y \rightarrow y'} \left( \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(u)) du \right).$$

743 Hence, by using (2.2) we have

$$744 \quad \left\| \frac{\hat{X}^{V,2\varepsilon}(u)}{V} - Z(u) \right\|_\infty \leq \left\| \frac{\hat{X}^{V,2\varepsilon}(0)}{V} - Z(0) \right\|_\infty + \frac{R}{V} \left| \sum_{y \rightarrow y' \in \mathcal{R}} \bar{N}_{y \rightarrow y'} \left( \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(w)) dw \right) \right|$$

$$745 \quad + \int_0^u \left| \sum_{y \rightarrow y' \in \mathcal{R}} \left( \frac{\lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(w))}{V} - \lambda_{y \rightarrow y'} \left( \frac{X^{V,2\varepsilon}(w)}{V} \right) \right) \right| dw$$

$$746 \quad + \int_0^u \left| \sum_{y \rightarrow y'} \left( \lambda_{y \rightarrow y'} \left( \frac{X^{V,2\varepsilon}(w)}{V} \right) - \lambda_{y \rightarrow y'}(Z(w)) \right) \right| dw$$

$$747 \quad \leq \left\| \frac{X^V(0)}{V} - Z(0) \right\|_\infty + \frac{R}{V} \left| \bar{U}^{V,2\varepsilon} \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(w)) dw \right) \right|$$

$$748 \quad + \delta_1^{V,2\varepsilon,u} + \int_0^u L_0^{2\varepsilon,w} \left\| \frac{X^{V,2\varepsilon}(w)}{V} - Z(w) \right\|_\infty dw$$

750 By using (A.2), by taking the supremum over  $[0, t]$  on both sides we obtain

$$751 \quad \sup_{0 \leq u \leq t} \left\| \frac{\hat{X}^{V,2\varepsilon}(u)}{V} - Z(u) \right\|_\infty \leq \left\| \frac{X^V(0)}{V} - Z(0) \right\|_\infty$$

$$752 \quad + \frac{R}{V} \sup_{0 \leq u \leq t} \left| \bar{U}^{V,2\varepsilon} \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(w)) dw \right) \right|$$

$$753 \quad + \delta_1^{V,2\varepsilon,t} + \int_0^t L_0^{2\varepsilon,u} \sup_{0 \leq w \leq u} \left\| \frac{\hat{X}^{V,2\varepsilon}(w)}{V} - Z(w) \right\|_\infty du.$$

754  
755 By Gronwall's inequality we get

$$756 \quad \sup_{0 \leq u \leq t} \left\| \frac{\hat{X}^{V,2\varepsilon}(t)}{V} - Z(t) \right\|_\infty \leq e^{L_1^{2\varepsilon,t}} \left\| \frac{X^V(0)}{V} - Z(0) \right\|_\infty$$

$$757 \quad + \frac{Re^{L_1^{2\varepsilon,t}}}{V} \sup_{0 \leq u \leq t} \left| \bar{U}^{V,2\varepsilon} \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,2\varepsilon}(w)) dw \right) \right|$$

$$758 \quad + e^{L_1^{2\varepsilon,t}} \delta_1^{V,2\varepsilon,t}.$$

760 By noting that for all  $t \in \mathbb{R}_{\geq 0}$

$$761 \quad \sup_{z \in \Omega_1^{2\varepsilon, t}} \sum_{y \rightarrow y' \in \mathcal{R}} \frac{\lambda_{y \rightarrow y'}^V([Vz])}{V} \leq \Lambda_0^{2\varepsilon, t} + \delta_0^{V, 2\varepsilon, t},$$

762 we get

$$763 \quad p^{V, \varepsilon, t} \leq P \left( e^{L_1^{2\varepsilon, t}} \left\| \frac{X^V(0)}{V} - Z(0) \right\|_{\infty} > (1 - \gamma)\varepsilon \right) \\ 764 \quad + P \left( \text{Re}^{L_1^{2\varepsilon, t}} \sup_{0 \leq u \leq V(\Lambda_1^{2\varepsilon, t} + \delta_1^{V, 2\varepsilon, t})} \left| \frac{\bar{U}^{V, 2\varepsilon}(u)}{V} \right| + e^{L_1^{2\varepsilon, t}} \delta_1^{V, 2\varepsilon, t} > \gamma\varepsilon \right)$$

766 for any  $\gamma$  in  $(0, 1]$ . the proof is concluded by Lemma A.1.  $\square$

767 *Example A.3.* Consider the SIS reaction network described in (4.2). In this case,  
768 in accordance with the classical mass-action choice of kinetics we have

$$769 \quad \lambda_{S+I \rightarrow 2I}^V(x) = \frac{1}{V} \kappa_1 x_S x_I \quad \text{and} \quad \lambda_{I \rightarrow S}^V(x) = \kappa_2 x_I$$

770 for some positive constants  $\kappa_1$  and  $\kappa_2$ . Hence, Assumption 3.1 is satisfied with

$$771 \quad \lambda_{S+I \rightarrow 2I}(z) = \kappa_1 z_S z_I \quad \text{and} \quad \lambda_{I \rightarrow S}(z) = \kappa_2 z_I.$$

772 The corresponding solution  $Z$  exists for all non-negative times  $t$ , for all initial condi-  
773 tions  $Z(0) = z^*$ . Moreover, note that the sum of infected and susceptible individuals  
774 is kept constant, hence for all  $t \in \mathbb{R}_{> 0}$  we have  $Z_S(t) + Z_I(t) = z_S^* + z_I^* = \|z^*\|_1$ . In  
775 this case we can obtain the following rough estimates

$$776 \quad R = 2, \quad \Lambda_0^{\varepsilon, t} \leq (\|z^*\|_1 + \varepsilon)[\kappa_1(\|z^*\|_1 + \varepsilon) + \kappa_2], \quad L_0^{\varepsilon, t} \leq \kappa_1(\|z^*\|_1 + \varepsilon) + \kappa_2, \\ 777 \quad \delta_0^{V, \varepsilon, t} = 0, \quad \eta^{V, \varepsilon, t} \geq \varepsilon e^{-t\kappa_1(\|z^*\|_1 + 2\varepsilon) + t\kappa_2}.$$

779 If we assume  $X^V(0) = Vz^*$ , then  $p^{V, 0, 0} = 0$ . It follows from Theorem A.2 with the  
780 choice  $\gamma = 1$  that in this case

$$781 \quad p^{V, \varepsilon, t} \leq 6 \exp \left( \frac{t}{2} (\|z^*\|_1 + 2\varepsilon) [\kappa_1(\|z^*\|_1 + 2\varepsilon) + \kappa_2] - \frac{\varepsilon \sqrt{V}}{6} e^{-t[\kappa_1(\|z^*\|_1 + 2\varepsilon) - \kappa_2]} \right),$$

782 where  $\exp(h)$  is defined as  $e^h$  for all real numbers  $h$ .

783 **A.2. Proof of Theorem 5.2.** First of all, we define some quantities that are  
784 useful to give specific bounds on our approximation error. Define

$$785 \quad \tilde{\Lambda}_0^t = \max_{\tilde{S} \in \tilde{\mathcal{X}}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, Z(t)), \\ 786 \quad \tilde{L}_0^{\varepsilon, t} = \sup_{\substack{(z, z') \in \Omega_2^{\varepsilon, t} \\ z \neq z'}} \max_{\tilde{S} \in \tilde{\mathcal{X}}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \frac{|\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z')|}{\|z - z'\|_{\infty}} \\ 787 \quad \tilde{\delta}_0^{\varepsilon, t} = \sup_{z \in \Omega_1^{\varepsilon, t}} \max_{\tilde{S} \in \tilde{\mathcal{X}}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} |\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\tilde{S}, [Vz]) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z)| \\ 788 \quad \tilde{\Lambda}_1^t = \int_0^t \tilde{\Lambda}_0^u du, \quad \tilde{L}_1^{\varepsilon, t} = \int_0^t L_0^{\varepsilon, u} du, \quad \tilde{\delta}_1^{\varepsilon, t} = \int_0^t \delta_0^{V, \varepsilon, u} du. \\ 789$$

790 Note that  $\tilde{\Lambda}_0^t$  is finite for any  $t \in [0, T]$ , due to the fact that  $Z$  is defined over the  
 791 whole interval  $[0, T]$ . Moreover the functions  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}$  are locally Lipschitz on  $\mathbb{R}_{>0}^d$   
 792 by Lemma 5.1, hence  $\tilde{L}_0^{\varepsilon, t}$  is finite for all  $t \in [0, T]$ . Finally,  $\tilde{\delta}_0^{V, \varepsilon, t}$  is finite for all  
 793  $t \in [0, T]$  by Lemma 5.1. Note that, for fixed  $V$  and  $\varepsilon$ , the quantities  $\tilde{L}_0^{\varepsilon, t}$  and  $\tilde{\delta}_0^{\varepsilon, t}$   
 794 are non-decreasing functions of  $t$ . As a consequence, for all  $t \in [0, T]$ ,  $\varepsilon \in \mathbb{R}_{>0}$ , and  
 795  $V \in \mathbb{Z}_{\geq 1}$  we have

$$796 \quad (\text{A.4}) \quad \tilde{\Lambda}_1^t \leq t\tilde{\Lambda}_0^t, \quad \tilde{L}_1^{\varepsilon, t} \leq t\tilde{L}_0^{\varepsilon, t}, \quad \text{and} \quad \tilde{\delta}_1^{\varepsilon, t} \leq t\tilde{\delta}_0^{\varepsilon, t}.$$

797 Before proving Theorem 5.2 we show the following stronger result.

798 **THEOREM A.4.** *Assume that Assumption 3.1 holds. Furthermore, assume that*  
 799 *the random variables  $X^V(0)/V$  converge in probability to a constant  $z^*$  as  $V$  goes to*  
 800 *infinity. Assume that the solution  $Z$  to (2.2) with  $Z(0) = z^*$  exists over the interval*  
 801  *$[0, T]$  and that*

$$802 \quad m = \min_{\substack{S \in \mathcal{X} \\ u \in [0, T]}} Z_S(u) > 0.$$

803 Finally, assume that  $Y^V(0) = Y(0)$  for all positive integers  $V$ . Then,

$$804 \quad (\text{A.5}) \quad P(Y^V(t) \neq Y(t)) = E[\|Y^V(t) - Y(t)\|_\infty].$$

805 Moreover, for any  $0 < \varepsilon < m$

$$806 \quad \sup_{t \in [0, T]} E[\|Y^V(t) - Y(t)\|_\infty] \leq p^{V, \varepsilon, T} + (\tilde{\delta}_1^{V, \varepsilon, T} + \varepsilon \tilde{L}_1^{\varepsilon, T}) e^{2\tilde{\Lambda}_1^T}.$$

807 *Proof.* First, note that

$$808 \quad (\text{A.6}) \quad \|Y^V(t) - Y(t)\|_\infty = \begin{cases} 1 & \text{if } Y^V(t) \neq Y(t) \\ 0 & \text{if } Y^V(t) = Y(t) \end{cases},$$

809 hence (A.5) holds. Consider the process

$$810 \quad \hat{Y}^V(t) = Y(0) + \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} (\tilde{S}' - \tilde{S}) N_{\tilde{S}+y \rightarrow \tilde{S}'+y'} \left( \int_0^t \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\hat{Y}^V(u), X^{V, \varepsilon}(u)) du \right). \quad \blacksquare$$

811 By equations (5.2) and (A.7), using the triangular inequality, we obtain

$$812 \quad E[\|\hat{Y}^V(t) - Y(t)\|_\infty] \\ 813 \quad \leq E \left[ \int_0^t \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\hat{Y}^V(u), X^{V, \varepsilon}(u)) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(Y(u), Z(u)) \right| du \right] \\ 814 \quad \leq \Upsilon_1 + \Upsilon_2 + \Upsilon_3 \quad \blacksquare$$

816 where

$$\begin{aligned}
817 \quad \Upsilon_1 &= E \left[ \int_0^t \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\hat{Y}^V(u), X^{V,\varepsilon}(u)) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'} \left( \hat{Y}^V(u), \frac{X^{V,\varepsilon}(u)}{V} \right) \right| du \right] \\
818 \quad \Upsilon_2 &= E \left[ \int_0^t \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'} \left( \hat{Y}^V(u), \frac{X^{V,\varepsilon}(u)}{V} \right) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\hat{Y}^V(u), Z(u)) \right| du \right] \\
819 \quad \Upsilon_3 &= E \left[ \int_0^t \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\hat{Y}^V(u), Z(u)) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(Y(u), Z(u)) \right| du \right]
\end{aligned}$$

821 Since for every  $\tilde{S} + y \rightarrow \tilde{S}' + y' \in \tilde{\mathcal{R}}$  we have

$$\begin{aligned}
822 \quad \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(w, x) &= \mathbb{1}_{\{\tilde{S}\}}(w) \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\tilde{S}, x) \quad \text{for all } x \in \mathbb{Z}_{\geq 0}^d, w \in \tilde{\mathcal{X}} \\
823 \quad \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(w, z) &= \mathbb{1}_{\{\tilde{S}\}}(w) \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z) \quad \text{for all } z \in \mathbb{R}_{\geq 0}^d, w \in \tilde{\mathcal{X}},
\end{aligned}$$

825 we can write  $\Upsilon_1 \leq \tilde{\delta}_1^{V,\varepsilon,t}$ . Similarly,  $\Upsilon_2 \leq \varepsilon \tilde{L}_1^{\varepsilon,t}$ . Finally,

$$\begin{aligned}
826 \quad \Upsilon_3 &= E \left[ \int_0^t \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \mathbb{1}_{\{\tilde{S}\}}(\hat{Y}^V(u)) - \mathbb{1}_{\{\tilde{S}\}}(Y(u)) \right| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, Z(u)) du \right] \\
827 \quad &\leq E \left[ \int_0^t \sum_{\tilde{S} \in \tilde{\mathcal{X}}} \left| \mathbb{1}_{\{\tilde{S}\}}(\hat{Y}^V(u)) - \mathbb{1}_{\{\tilde{S}\}}(Y(u)) \right| \tilde{\Lambda}_0^u du \right] \\
828 \quad &= \int_0^t 2P(Y^V(u) \neq Y(u)) \tilde{\Lambda}_0^u du = 2 \int_0^t E \left[ \|\hat{Y}^V(u) - Y(u)\|_\infty \right] \tilde{\Lambda}_0^u du,
\end{aligned}$$

830 where in the last equality we used (A.5). In conclusion,

$$831 \quad E \left[ \|\hat{Y}^V(t) - Y(t)\|_\infty \right] \leq (\tilde{\delta}_1^{V,\varepsilon,t} + \varepsilon \tilde{L}_1^{\varepsilon,t}) + 2 \int_0^t E \left[ \|\hat{Y}^V(u) - Y(u)\|_\infty \right] \tilde{\Lambda}_0^u du.$$

832 By the Gronwall inequality we then have

$$833 \quad E \left[ \|\hat{Y}^V(t) - Y(t)\|_\infty \right] \leq (\tilde{\delta}_1^{V,\varepsilon,t} + \varepsilon \tilde{L}_1^{\varepsilon,t}) e^{2\tilde{\Lambda}_1^t}.$$

834 The result follows by taking the sup over  $t \in [0, T]$  on both sides (the quantity  
835 on the right-hand side of the inequality is non-decreasing in  $t$ ) and by noting that  
836  $\mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}} \hat{Y}^V(t) = \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}} Y^V(t)$  for all  $t \in [0, T]$ . Hence,

$$\begin{aligned}
837 \quad \|\hat{Y}^V(t) - Y(t)\|_\infty &= \|Y^V(t) - Y(t)\|_\infty \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}^c} + \|\hat{Y}^V(t) - Y(t)\|_\infty \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}} \\
838 \quad &\leq \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}^c} + \|\hat{Y}^V(t) - Y(t)\|_\infty \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}} \\
839 \quad &\leq \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}^c} + \|\hat{Y}^V(t) - Y(t)\|_\infty. \quad \square
\end{aligned}$$

841 We are now ready to prove Theorem 5.2

842 *Proof of Theorem 5.2.* It follows from Theorem A.4 that  $P(Y^V(t) \neq Y(t)) =$   
 843  $E[\|Y^V(t) - Y(t)\|_\infty]$ . Moreover, for any  $\varepsilon > 0$  we have  $\lim_{V \rightarrow \infty} p^{V,\varepsilon,T} = 0$  by  
 844 Theorem 3.2, and  $\lim_{V \rightarrow \infty} \tilde{\delta}_1^{V,\varepsilon,T} = 0$  by Lemma 5.1 and (A.4). Hence,

$$845 \quad \lim_{V \rightarrow \infty} \sup_{t \in [0, T]} E[\|Y^V(t) - Y(t)\|_\infty] \leq \varepsilon \tilde{L}_1^{\varepsilon, T} e^{2\tilde{\Lambda}_1^T},$$

846 which concludes the proof by the arbitrariness of  $\varepsilon > 0$  and by the fact that  $\tilde{L}_0^{\varepsilon, T}$   
 847 (hence  $\tilde{L}_1^{\varepsilon, T}$ ) is non-decreasing in  $\varepsilon$ .  $\square$

848 **A.3. Proof of Theorem 5.8.** Similarly to what was done in the previous section,  
 849 we define the following quantities to give an upper bound for our approximation  
 850 error. Define

$$851 \quad \hat{R} = \max_{y \rightarrow y' \in \mathcal{R}} \|\pi(y' - y)\|_\infty, \quad \hat{r} = \max_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left\| \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} - \frac{\tau(\tilde{S})}{\alpha(\tau(\tilde{S}))} \right\|_\infty,$$

$$852 \quad \hat{\Lambda}_0^t = \hat{r} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, Z(t)), \quad \hat{\Lambda}_1^t = \int_0^t \hat{\Lambda}_0^u du,$$

$$853 \quad \hat{\Lambda}_2^t = \max_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \int_0^t \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, Z(u)) du,$$

$$854 \quad \hat{\Lambda}_3^{V,\varepsilon,t} = \int_0^t \sup_{z \in \Omega_1^{\varepsilon,u}} \sum_{y \rightarrow y' \in \mathcal{R}} \frac{\lambda_{y \rightarrow y'}(\lfloor Vz \rfloor)}{V} du,$$

$$855 \quad \omega^{\varepsilon,t} = \hat{r} \sup_{\substack{(z,z') \in \Omega_2^{\varepsilon,t} \\ \|z-z'\|_\infty \leq \varepsilon}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \left| \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z) - \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}(\tilde{S}, z') \right|,$$

$$856 \quad \zeta^{\varepsilon,t} = \int_0^t (\|Z(u)\|_\infty + \varepsilon) du.$$

858 Note that  $\hat{\Lambda}_0^t$ ,  $\hat{\Lambda}_2^t$ , and  $\zeta^{\varepsilon,t}$  are finite for any  $t \in [0, T]$ , because  $Z$  is defined  
 859 over the whole interval  $[0, T]$  and the functions  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}$  are continuous on  $\mathbb{R}_{>0}^d$  by  
 860 Lemma 5.1. Lemma 5.1 also implies that  $\omega^{\varepsilon,t}$  is finite for all  $t \in [0, T]$  and  $\varepsilon \in \mathbb{R}_{>0}$ .  
 861 Finally,  $\hat{\Lambda}_3^{V,\varepsilon,t}$  is finite by Assumption 3.1. Note that, for fixed  $V$  and  $\varepsilon$ , the quantities  
 862  $\hat{\Lambda}_3^{V,\varepsilon,t}$ ,  $\omega^{\varepsilon,t}$ , and  $\zeta^{\varepsilon,t}$  are non-decreasing functions of  $t$ .

863 We now state and prove the following result, which immediately implies Theorem  
 864 5.8. Note that  $\delta_1^{V,\varepsilon,t}$  is as defined in Section A.1.

865 **THEOREM A.5.** *Consider a family of stochastic reaction systems with trackable*  
 866 *species  $(Y^V, X^V)$ , and assume that Assumptions 3.1 and 5.6 are satisfied. Let  $z^* \in$*   
 867  *$\mathbb{R}_{>0}^d$  and  $\tilde{X}^V(0) = \lfloor Vz^* \rfloor$ . Define the process  $\tilde{X}^V$  by*

$$868 \quad \tilde{X}^V(t) = \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \frac{\tau(Y^{\tilde{S},i}(t))}{\alpha(\tau(Y^{\tilde{S},i}(t)))},$$

869 where the processes  $(Y^{\tilde{S},i})_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}, i \in \mathbb{Z}_{\geq 1}}$  are independent and satisfy

$$870 \quad Y^{\tilde{S},i}(t) = \tilde{S} + \sum_{\tilde{S}'+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} (\tilde{S}'' - \tilde{S}') N_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}^{\tilde{S},i} \left( \int_0^t \lambda_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}(Y(u)^{\tilde{S},i}, Z(u)) du \right),$$

871 for a family of independent, identically distributed unit-rate Poisson processes  $\{N_r^{\tilde{S},i}\}_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}, i \in \mathbb{Z}_{\geq 1}, r \in \tilde{\mathcal{R}}}$  ■  
 872 For arbitrary  $\nu_1, \nu_2, \nu_3 \in \mathbb{R}_{>0}$  define

$$873 \quad \nu = e^{\hat{\Lambda}_1^T} \left( \hat{R}\nu_1 + \hat{r}\nu_2 + \nu_3 + \hat{R}\delta_1^{V,\varepsilon,T} + \omega^{\varepsilon,T}\zeta^{\varepsilon,T} \right)$$

874 Then,

$$875 \quad P \left( \sup_{0 \leq t \leq T} \left\| \frac{\pi(X^V(t))}{V} - \frac{\tilde{X}^V(t)}{V} \right\|_{\infty} > \nu \right) \leq 6 \exp \left( \frac{e\hat{\Lambda}_3^{V,\varepsilon,t}}{2} - \frac{\nu_1\sqrt{V}}{3} \right)$$

$$877 \quad + 6 \exp \left( \frac{ec\hat{\Lambda}_2^t}{2} - \frac{\nu_2\sqrt{V}}{3} \right) + P \left( \left\| \frac{\pi(X^V(0))}{V} - \frac{\tilde{X}^V(0)}{V} \right\|_{\infty} > \nu_3 \right) + p^{V,\varepsilon,T},$$

878

879 where  $c = \sum_{S \in \mathcal{X}} \alpha(S)z_S^*$ .

880 *Proof.* By the superposition property of Poisson processes, for all  $V \in \mathbb{Z}_{\geq 1}$  there  
 881 exist two unit-rate Poisson processes  $U_1^V$  and  $U_2^V$  such that for all  $t \in \mathbb{R}_{\geq 0}$

$$882 \quad U_1^V \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \right) = \sum_{y \rightarrow y' \in \mathcal{R}} N_{y \rightarrow y'} \left( \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \right)$$

883 and

$$884 \quad U_2^V \left( \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \int_0^t \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(u), Z(u)) du \right)$$

$$886 \quad = \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} N_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}^{\tilde{S},i} \left( \int_0^t \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(u), Z(u)) du \right)$$

887 ■

888 Note that

$$889 \quad \tilde{X}^V(t) = \tilde{X}^V(0) + \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \times$$

$$891 \quad \times N_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}^{\tilde{S},i} \left( \int_0^t \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y(u)^{\tilde{S},i}, Z(u)) du \right).$$

892

893 Hence, by triangular inequality,

$$894 \quad \sup_{0 \leq u \leq t} \left\| \frac{\pi(\hat{X}^{V,\varepsilon}(u))}{V} - \frac{\tilde{X}^V(u)}{V} \right\|_{\infty} \leq \left\| \frac{\pi(X^V(0))}{V} - \frac{\tilde{X}^V(0)}{V} \right\|_{\infty} + \sum_{i=1}^5 \Upsilon_i$$

895

896 where

$$\begin{aligned}
897 \quad \Upsilon_1 &= \sup_{0 \leq u \leq t} \sum_{y \rightarrow y' \in \mathcal{R}} \|\pi(y' - y)\|_\infty \frac{1}{V} \left| \bar{N}_{y \rightarrow y'} \left( \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(w)) dw \right) \right| \\
898 \quad &\leq \frac{\hat{R}}{V} \sup_{0 \leq u \leq t} \left| \bar{U}_1^V \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^u \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(w)) dw \right) \right| \\
899 \quad \Upsilon_2 &= \sup_{0 \leq u \leq t} \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \left\| \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right\|_\infty \times \\
900 \quad &\times \frac{1}{V} \left| \bar{N}_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}^{\tilde{S},i} \left( \int_0^u \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(w), Z(w)) dw \right) \right| \\
901 \quad &\leq \frac{\hat{r}}{V} \sup_{0 \leq u \leq t} \left| \bar{U}_2^V \left( \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \int_0^u \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(w), Z(w)) dw \right) \right| \\
902 \quad \Upsilon_3 &= \sup_{0 \leq u \leq t} \sum_{y \rightarrow y' \in \mathcal{R}} \|\pi(y' - y)\|_\infty \int_0^u \left| \frac{\lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(w))}{V} - \lambda_{y \rightarrow y'} \left( \frac{X^{V,\varepsilon}(w)}{V} \right) \right| dw \\
903 \quad &\leq \hat{R} \delta_1^{V,\varepsilon,t} \\
904 \quad \Upsilon_4 &= \sup_{0 \leq u \leq t} \left\| \sum_{y \rightarrow y' \in \mathcal{R}} \pi(y' - y) \int_0^u \lambda_{y \rightarrow y'} \left( \frac{X^{V,\varepsilon}(w)}{V} \right) dw \right. \\
905 \quad &\quad \left. - \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \int_0^u \frac{X_{\tau(\tilde{S}')}^{V,\varepsilon}(w)}{V} \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(\tilde{S}', Z(w)) dw \right\|_\infty \\
906 \quad \Upsilon_5 &= \sup_{0 \leq u \leq t} \left\| \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \int_0^u \frac{X_{\tau(\tilde{S}')}^{V,\varepsilon}(w)}{V} \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(\tilde{S}', Z(w)) dw \right. \\
907 \quad &\quad \left. - \frac{1}{V} \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \int_0^u \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(w), Z(w)) dw \right\|_\infty \blacksquare
\end{aligned}$$

909 We first focus on rewriting  $\Upsilon_4$  and  $\Upsilon_5$ . To this aim, first note that by identifying  
910 species with canonical vectors of  $\mathbb{R}^d$  as previously done in the paper, we have that for  
911 all  $y \in \mathcal{C}$

$$912 \quad \pi(y) = \sum_{S \in \bar{\mathcal{X}}} y_S S = \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{y_{\tau(\tilde{S})} \tau(\tilde{S})}{\alpha(\tau(\tilde{S}))}.$$

913 Hence, for all  $y \rightarrow y' \in \mathcal{R}$

$$\begin{aligned}
914 \quad \pi(y' - y) &= \sum_{\tilde{S}' \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{y_{\tau(\tilde{S}')\tau(\tilde{S}')}}{\alpha(\tau(\tilde{S}'))} - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{y_{\tau(\tilde{S})\tau(\tilde{S})}}{\alpha(\tau(\tilde{S}))} \\
915 \quad &= \sum_{\tilde{S}' \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})p_{y \rightarrow y'}(\tilde{S}, \tilde{S}')} - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{y_{\tau(\tilde{S})}}{\alpha(\tau(\tilde{S}))} \tau(\tilde{S}), \\
916
\end{aligned}$$

917 where we used Assumption 5.6 in the last equality. By recalling that  $\tau(\Delta) = 0$  and  
918  $\sum_{\tilde{S}' \in \tilde{\mathcal{X}}} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}')$  for all  $y \rightarrow y' \in \mathcal{R}$  and  $\tilde{S} \in \tilde{\mathcal{X}}$ , we further obtain

$$\begin{aligned}
919 \quad \pi(y' - y) &= \sum_{\tilde{S}' \in \tilde{\mathcal{X}}} \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} y_{\tau(\tilde{S})p_{y \rightarrow y'}(\tilde{S}, \tilde{S}')} \\
920 \quad &\quad - \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \frac{y_{\tau(\tilde{S})}}{\alpha(\tau(\tilde{S}))} \tau(\tilde{S}) \sum_{\tilde{S}' \in \tilde{\mathcal{X}}} p_{y \rightarrow y'}(\tilde{S}, \tilde{S}') \\
921 \quad &= \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}' \in \tilde{\mathcal{X}}} \left( \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} - \frac{\tau(\tilde{S})}{\alpha(\tau(\tilde{S}))} \right) y_{\tau(\tilde{S})p_{y \rightarrow y'}(\tilde{S}, \tilde{S}')}. \\
922
\end{aligned}$$

923 It follows that

$$\begin{aligned}
924 \quad \sum_{y \rightarrow y' \in \mathcal{R}} \pi(y' - y) \int_0^u \lambda_{y \rightarrow y'} \left( \frac{X^{V,\varepsilon}(w)}{V} \right) dw \\
925 \quad &= \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \int_0^u y_{\tau(\tilde{S}')p_{y \rightarrow y'}(\tilde{S}', \tilde{S}'')} \lambda_{y \rightarrow y'} \left( \frac{X^{V,\varepsilon}(w)}{V} \right) dw \\
926 \quad &= \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \left( \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right) \int_0^u \frac{X^{V,\varepsilon}_{\tau(\tilde{S}')} (w)}{V} \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'} \left( \tilde{S}', \frac{X^{V,\varepsilon}(w)}{V} \right) dw, \\
927
\end{aligned}$$

928 which in turn implies

$$\begin{aligned}
929 \quad \Upsilon_4 &\leq \sup_{0 \leq u \leq t} \sum_{\tilde{S}' + y \rightarrow \tilde{S}'' + y' \in \tilde{\mathcal{R}}} \left\| \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right\|_{\infty} \times \\
930 \quad &\quad \times \int_0^u \frac{X^{V,\varepsilon}_{\tau(\tilde{S}')} (w)}{V} \left| \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'} \left( \tilde{S}', \frac{X^{V,\varepsilon}(w)}{V} \right) - \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(\tilde{S}', Z(w)) \right| dw \\
931 \quad &\leq \omega^{\varepsilon,t} \zeta^{\varepsilon,t}.
\end{aligned}$$

933 By summing over the values of the single-molecule trajectories, we also have

$$\begin{aligned}
934 \\
935 \quad \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(Y^{\tilde{S},i}(w), Z(w)) = \tilde{X}_{\tau(\tilde{S})}^V(w) \lambda_{\tilde{S}' + y \rightarrow \tilde{S}'' + y'}(\tilde{S}, Z(w)), \\
936
\end{aligned}$$

937 which implies

$$\begin{aligned}
938 \quad \Upsilon_5 &\leq \sup_{0 \leq u \leq t} \sum_{\tilde{S}'+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} \left\| \frac{\tau(\tilde{S}'')}{\alpha(\tau(\tilde{S}''))} - \frac{\tau(\tilde{S}')}{\alpha(\tau(\tilde{S}'))} \right\|_{\infty} \int_0^u \left| \frac{X_{\tau(\tilde{S})}^{V,\varepsilon}(w)}{V} - \frac{\tilde{X}_{\tau(\tilde{S})}^V(w)}{V} \right| \lambda_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}(\tilde{S}', Z(w)) dw \\
939 &\leq \int_0^t \left\| \frac{X^{V,\varepsilon}(u)}{V} - \frac{\tilde{X}^V(u)}{V} \right\|_{\infty} \hat{\Lambda}_0^u du \\
940 &= \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}^c} \int_0^t \left\| \frac{X^{V,\varepsilon}(u)}{V} - \frac{\tilde{X}^V(u)}{V} \right\|_{\infty} \hat{\Lambda}_0^u du + \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}} \int_0^t \left\| \frac{\hat{X}^{V,\varepsilon}(u)}{V} - \frac{\tilde{X}^V(u)}{V} \right\|_{\infty} \hat{\Lambda}_0^u du. \\
941 &\leq \mathbb{1}_{\mathcal{A}_{V,\varepsilon,t}^c} M^{V,\varepsilon,t} + \int_0^t \left\| \frac{\hat{X}^{V,\varepsilon}(u)}{V} - \frac{\tilde{X}^V(u)}{V} \right\|_{\infty} \hat{\Lambda}_0^u du, \\
942 &
\end{aligned}$$

943 where

$$944 \quad M^{V,\varepsilon,t} = \int_0^t \left( \|Z(u)\|_{\infty} + \varepsilon + \sum_{S \in \mathcal{X}} \alpha(S) \frac{\tilde{X}_S^V(0)}{V} \right) \hat{\Lambda}_0^u du$$

945 is an almost surely finite random variable, non-decreasing in  $t$ . Hence, putting every-  
946 thing together and applying the Gronwall inequality we have that almost surely

$$\begin{aligned}
947 \quad \sup_{0 \leq t \leq T} \left\| \frac{\pi(\hat{X}^{V,\varepsilon}(t))}{V} - \frac{\tilde{X}^V(t)}{V} \right\|_{\infty} &\leq e^{\hat{\Lambda}_1^T} \frac{\hat{R}}{V} \sup_{0 \leq t \leq T} \left| \bar{U}_1^V \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \right) \right| \\
948 &+ e^{\hat{\Lambda}_1^T} \frac{\hat{r}}{V} \sup_{0 \leq t \leq T} \left| \bar{U}_2^V \left( \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}'+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \int_0^t \lambda_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}(Y^{\tilde{S},i}(u), Z(u)) du \right) \right| \\
949 &+ e^{\hat{\Lambda}_1^T} \left( \left\| \frac{\pi(X^V(0))}{V} - \frac{\tilde{X}^V(0)}{V} \right\|_{\infty} + \hat{R} \delta_1^{V,\varepsilon,T} + \omega^{\varepsilon,T} \zeta^{\varepsilon,T} + \mathbb{1}_{\mathcal{A}_{V,\varepsilon,T}^c} M^{V,\varepsilon,T} \right). \\
950 &
\end{aligned}$$

951 Now note that if  $A_1, A_2, \dots, A_j$  are random variables and  $a_1, a_2, \dots, a_j$  are positive  
952 real numbers, then

$$953 \quad P \left( \sum_{i=1}^j A_i > \sum_{i=1}^j a_i \right) \leq P \left( \bigcup_{i=1}^j (A_i > a_i) \right) \leq \sum_{i=1}^j P(A_i > a_i).$$

954 Hence, if  $\nu$  is as in the statement of the theorem and  $\nu < \varepsilon$ ,

$$\begin{aligned}
955 \quad P \left( \sup_{0 \leq t \leq T} \left\| \frac{\pi(X^V(t))}{V} - \frac{\tilde{X}^V(t)}{V} \right\|_{\infty} > \nu \right) &= P \left( \sup_{0 \leq t \leq T} \left\| \frac{\pi(\hat{X}^{V,\varepsilon}(t))}{V} - \frac{\tilde{X}^V(t)}{V} \right\|_{\infty} > \nu \right) \\
956 &\leq P \left( \frac{1}{V} \sup_{0 \leq t \leq T} \left| \bar{U}_1^V \left( \sum_{y \rightarrow y' \in \mathcal{R}} \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \right) \right| > \nu_1 \right) \\
957 &+ P \left( \frac{1}{V} \sup_{0 \leq t \leq T} \left| \bar{U}_2^V \left( \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}'+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \int_0^t \lambda_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}(Y^{\tilde{S},i}(u), Z(u)) du \right) \right| > \nu_2 \right) \\
958 &+ p^{V,\varepsilon,T}. \\
959 &
\end{aligned}$$

960 Since for all  $t \in [0, T]$

$$961 \quad \int_0^t \lambda_{y \rightarrow y'}^V(X^{V,\varepsilon}(u)) du \leq V \hat{\Lambda}_3^{V,\varepsilon,t}$$

962 and

$$963 \quad \sum_{\tilde{S} \in \tilde{\mathcal{X}} \setminus \{\Delta\}} \sum_{\tilde{S}'+y \rightarrow \tilde{S}''+y' \in \tilde{\mathcal{R}}} \sum_{i=1}^{\tilde{X}_{\tau(\tilde{S})}^V(0)} \int_0^t \lambda_{\tilde{S}'+y \rightarrow \tilde{S}''+y'}(Y^{\tilde{S},i}(u), Z(u)) du \leq V c \hat{\Lambda}_2^t,$$

964 the proof is concluded by Lemma A.1.  $\square$

965 *Proof of Theorem 5.8.* Note that by Lemma 5.7 and by the fact that  $\alpha(S) \geq 1$   
966 for all  $S \in \mathcal{X}$  in (5.6),

$$967 \quad \left\| \frac{\pi(X^V(h))}{V} - \frac{\tilde{X}^V(h)}{V} \right\|_1 \leq \left\| \frac{\pi(X^V(h))}{V} \right\|_1 + \left\| \frac{\tilde{X}^V(h)}{V} \right\|_1$$

$$968 \quad \leq \frac{1}{V} \left( \sum_{S \in \tilde{\mathcal{X}}} \alpha(S) \left( X_S^V(0) + \tilde{X}_S^V(0) \right) \right).$$

969

970 Under the assumption that both  $X^V(0)$  and  $\tilde{X}^V(0)$  have finite expectation and con-  
971 verge in probability to  $z^*$ , and by the equivalence of norms in finite dimension, we  
972 conclude there exists  $M \in \mathbb{R}_{>0}$  such that

$$973 \quad \sup_{V \in \mathbb{Z}_{\geq 1}} E \left[ \left\| \frac{\pi(X^V(h))}{V} - \frac{\tilde{X}^V(h)}{V} \right\|_\infty \right] \leq M.$$

974 Hence, if  $\nu$  is as in Theorem A.5, we have that

$$975 \quad E \left[ \sup_{0 \leq t \leq T} \left\| \frac{\pi(X^V(h))}{V} - \frac{\tilde{X}^V(h)}{V} \right\|_\infty \right] \leq \nu + 6M e^{\frac{\hat{\Lambda}_3^{V,\varepsilon,t}}{2} - \frac{\nu_1 \sqrt{V}}{3}}$$

$$976 \quad + 6M e^{\frac{c \hat{\Lambda}_2^t}{2} - \frac{\nu_2 \sqrt{V}}{3}} + MP \left( \left\| \frac{\pi(X^V(0))}{V} - \frac{\tilde{X}^V(0)}{V} \right\|_\infty > \nu_3 \right) + Mp^{V,\varepsilon,T}.$$

977

978

979 The proof is concluded if we can show that for all  $T \in \mathbb{R}_{>0}$  and any arbitrary  $\eta > 0$ ,  
980 we can fix  $\nu_1, \nu_2, \nu_3 \in \mathbb{R}_{>0}$  and  $\varepsilon \in (0, m)$  such that  $\nu < \eta$  for large enough values  
981 of  $V$ . Indeed, for any fixed  $\varepsilon \in (0, m), T \in \mathbb{R}_{>0}$  the other terms on the right-hand  
982 side of the above inequality tend to zero as  $V$  goes to infinity. To show that  $\nu$  can  
983 be made smaller than  $\eta$ , simply note that  $\nu_1, \nu_2, \nu_3$  can be chosen as small as desired  
984 among the positive real numbers,  $\delta_1^{V,\varepsilon,T}$  tends to zero as  $V$  goes to infinity for all fixed  
985  $\varepsilon \in (0, m)$  by Assumption 3.1, and  $\omega^{\varepsilon,T}$  tends to zero as  $\varepsilon$  tends to zero because the  
986 functions  $\lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}$  are locally Lipschitz on  $\tilde{\mathcal{X}} \times \mathbb{R}_{>0}^d$  by Lemma 5.1.  $\square$

987 **A.4. Proof of Theorem 5.5.** Note that under the assumptions of Theorem 5.5,  
988 for all  $t \in [0, T]$   $Y^V(t)$  converges in probability to  $Y(t)$  by Theorem 5.2. Hence, in  
989 order to prove Theorem 5.5, we need to show relative compactness of  $\{Y^V\}$  as a  
990 sequence of processes with sample paths in  $D_{\tilde{\mathcal{X}}}[0, T]$ , and conclude by [10, Lemma  
991 A2.1]. To prove relative compactness of  $\{Y^V\}$ , first note that the state space  $\tilde{\mathcal{X}}$  is

compact. Hence, we only need to show that the jump times do not accumulate as  $V$  tends to infinity, nor tend to 0. Let  $t_i^V$  with  $i \in \mathbb{Z}_{\geq 1}$  denote the time of the  $i$ th jump of  $Y^V$ , let  $t_0^V = 0$ , and let  $T^V$  be the time of the last jump of  $Y^V$  in  $[0, T]$ . Fix  $\delta \in \mathbb{R}_{>0}$  and for all  $j \in \mathbb{Z}$  with  $-1 \leq j \leq T/\delta$  let  $N_j^{V,\delta}$  be the number of jumps of  $Y^V$  in the interval  $[j/\delta, \min\{j/\delta + 2\delta, T\}]$ . The  $N_j^{V,\delta}$  are introduced to control the time between jumps: whenever two jumps occur at times closer than  $\delta$ , there necessarily exists an interval  $[j/\delta, \min\{j/\delta + 2\delta, T\}]$  with  $j \geq 0$  containing both of them. Also, whenever the time of a jump is smaller than 0, then  $N_{-1}^{V,\delta} \geq 1$ . Hence, for all  $\varepsilon \in \mathbb{R}_{>0}$  with  $\varepsilon > m$ ,

$$\begin{aligned} P\left(\min_{j=1,\dots,T^V}(t_j^V - t_{j-1}^V) \leq \delta\right) &\leq P\left(N_{-1}^{V,\delta} \geq 1 \text{ or } \max_{j=1,\dots,\lfloor T/\delta \rfloor} N_j^{V,\delta} \geq 2\right) \\ &\leq P\left(N_{-1}^{V,\delta} \geq 1\right) + \sum_{j=1}^{\lfloor T/\delta \rfloor} P(N_j^{V,\delta} \geq 2) \\ &\leq P\left(\sup_{0 \leq t \leq T} \left\| \frac{X^V}{V}(t) - Z(t) \right\|_{\infty} > \varepsilon\right) + P(N^\varepsilon(\delta) \geq 1) + \frac{T}{\delta} P(N^\varepsilon(2\delta) \geq 2), \end{aligned}$$

where  $N^\varepsilon$  is a Poisson process with rate

$$B_\varepsilon = \sup_{N \in \mathbb{Z}_{\geq 1}} \sup_{z \in \Omega_1^{\varepsilon,T}} \max_{\tilde{S} \in \tilde{\mathcal{X}}} \sum_{\tilde{S}+y \rightarrow \tilde{S}'+y' \in \tilde{\mathcal{R}}} \lambda_{\tilde{S}+y \rightarrow \tilde{S}'+y'}^V(\tilde{S}, [Vz]),$$

which is finite by Lemma 5.1. Hence, by Theorem 3.2

$$\limsup_{V \rightarrow \infty} P\left(\min_{j=1,\dots,T^V}(t_j^V - t_{j-1}^V) \leq \delta\right) \leq (1 - e^{-\delta B_\varepsilon}) + \frac{T}{\delta} (1 - e^{-2\delta B_\varepsilon} - 2\delta B_\varepsilon e^{-2\delta B_\varepsilon}),$$

which tends to 0 as  $\delta$  tends to 0. Therefore,  $\{Y^V\}$  is relatively compact as a sequence of processes with sample paths in  $D_{\tilde{\mathcal{X}}}[0, T]$  by [11, Corollary 7.4, Chapter 3], which completes the proof.

1012

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