Anomalous kinetics in diffusion limited reactions linked to non-Gaussian concentration probability distribution function

Pietro de Anna,[1,a)] Tanguy Le Borgne,[1] Marco Dentz,[2] Diogo Bolster,[3] and Philippe Davy[1]

[1]*Laboratoire Géosciences Rennes, Unité Mixte de Recherche CNRS Université de Rennes 1, F-35042 Rennes Cedex, France*

[2]*Institute of Environmental Assessment and Water Research, Consejo Superior de Investigaciones Científicas, Barcelona, Spain*

[3]*Environmental Fluid Dynamics Laboratory, University of Notre Dame, South Bend, Indiana 46556, USA*

We investigate anomalous reaction kinetics related to segregation in the one-dimensional reaction-diffusion system $A + B \rightarrow C$. It is well known that spatial fluctuations in the species concentrations cause a breakdown of the mean-field behavior at low concentration values. The scaling of the average concentration with time changes from the mean-field t^{-1} to the anomalous $t^{-1/4}$ behavior. Using a stochastic modeling approach, the reaction-diffusion system can be fully characterized by the multi-point probability distribution function (PDF) of the species concentrations. Its evolution is governed by a Fokker-Planck equation with moving boundaries, which are determined by the positivity of the species concentrations. The concentration PDF is in general non-Gaussian. As long as the concentration fluctuations are small compared to the mean, the PDF can be approximated by a Gaussian distribution. This behavior breaks down in the fluctuation dominated regime, for which anomalous reaction kinetics are observed. We show that the transition from mean field to anomalous reaction kinetics is intimately linked to the evolution of the concentration PDF from a Gaussian to non-Gaussian shape. This establishes a direct relationship between anomalous reaction kinetics, incomplete mixing and the non-Gaussian nature of the concentration PDF. © *2011 American Institute of Physics.* [doi:10.1063/1.3655895]

I. INTRODUCTION

Reaction kinetics in heterogeneous reaction-diffusion systems are in general different from the ones observed in well-mixed reactors. Spatial fluctuations in species concentrations in conjunction with diffusion and chemical reactions can have a dramatic impact on the global reaction kinetics.[1–8] Mass transfer limitations can lead to reduced reactivity of the reaction system and slow down the global reaction kinetics.[9] The systematic quantification of the dynamics leading to this behavior is of scientific[1–3,10–12] as well of practical interest for all applications that involve chemical reactions in heterogeneous environments. In natural systems the spatial distribution of reactant concentrations is in general heterogeneous due to fluctuations of the host media that can be represented by porous media,[9,13–15] living cells,[16,17] and turbulent and chaotic flows,[18,19] for example. We focus here on the bimolecular irreversible reaction,

$$A + B \rightarrow C, \tag{1}$$

between species A and B which diffuse in one-dimensional space. The host medium is assumed to be homogeneous and transport is limited to molecular diffusion. The classical approach to describe such a reaction-diffusion system is by the combination of mass transfer for each species concentration $\phi_i(x, t)$ $(i = A, B)$ and a reaction term such that

$$\frac{\partial \phi_i(x, t))}{\partial t} - D \frac{\partial^2 \phi_i(x, t)}{\partial x^2} = -k\phi_A(x, t)\phi_B(x, t), \tag{2}$$

with D is the diffusion coefficient and k is the reaction rate constant. This description is valid in the mean-field limit of an infinite system size, that is, for an infinite number of particles of A and B. For a uniform initial distribution of both species in a closed reactor, $\phi_i(x, t = 0) = c_i$, (2) reduces to the rate equation,

$$\frac{d\phi_i(t)}{dt} = -k\phi_A(t)\phi_B(t). \tag{3}$$

At long times, the species concentrations decrease as t^{-1}. This behavior can be observed if (i) both species are well-mixed and (ii) the number of particles is infinite. In the presence of spatial heterogeneities (which can lead to incomplete mixing on a local scale) and for finite numbers of particles of A and B, this behavior can change. In natural systems, the number of constituents is finite. Therefore, stochastic deviations from the thermodynamic limit arise and the species concentrations are subject to random fluctuations.[20] The thermodynamic limit effectively prevents the formation of zones where only one reactant is present, and where reactions stop, because neither species A nor species B can completely deplete. Due to the creation of such a zones, or islands of non-reactive particles, the system is no longer well-mixed and diffusion effects start to play an important role and will dominate the kinetics of the system. While diffusion attenuates initial concentration contrasts, chemical reaction can

a)Electronic mail: pietro.deanna@univ-rennes1.fr.

amplify them by depleting the species concentrations wherever they are in contact. This leads to segregation, the formation of islands of the respective species. In this regime, the behavior of the species concentrations shows the characteristic $t^{-1/4}$ scaling.[1–3] Kang and Redner[3] used a scaling approach to characterize the anomalous evolution of the species concentrations caused by mass transfer limitations in conjunction with reaction. An analogous scaling has been shown to occur in super-diffusive Levy-flight reaction system.[12, 21, 22] In this case, the mean concentration scales asymptotically as $t^{-1/2\gamma}$, where $1 < \gamma < 2$ characterizes the Levy-enhanced diffusion operator. Furthermore, the breakdown of the mean-field description has been studied for variety of reaction diffusion systems using lattice gas automata approaches.[11]

In this paper, we study this fluctuation phenomenon from a different perspective. We focus on the description of the reaction diffusion system in terms of the joint concentration PDF of the chemical species and study its evolution as the reaction behavior changes from the mean field to the anomalous scaling. The concentration PDF encodes the full statistical information of the fluctuations of the species concentrations about the mean-field limit. Thus, it quantifies the uncertainty of the concentration values predicted by the mean field. At the same time, it allows for the systematic quantification of the impact of concentration fluctuations on the average behavior.

We employ a stochastic approach based on population dynamics,[23, 24, 27–29] which can be used for deriving the master equation for the concentration pdf. This framework has been used for the analysis of complex systems that show spontaneous deviations from the average behavior such as proteins and molecules in living cells[27, 28, 30] and predator-prey systems.[23, 31, 32] The system state is fully characterized by the joint PDF of the species concentrations at any point in space and time. Its evolution is governed by a reaction-diffusion master equation (RDME).[29, 30, 33–35] Using the van Kampen system size expansion, we derive at the first order a set of differential equations for the behavior of the system in the mean-field limit. Expanding the RDME up to the second order, we derive a Fokker-Plank equation for concentration fluctuations that quantifies the evolution of the joint concentration PDF through advective and diffusive probability fluxes in the multi-dimensional space of the concentration fluctuations. When the concentration fluctuations are small compared to the average, the PDF can be approximated by a multi-variate Gaussian distribution. This approximation, however, breaks down in the regime in which fluctuations dominate, that is, when the reaction kinetics show anomalous scaling. We study the evolution of the concentration PDF from a Gaussian to non-Gaussian shape due to the impact of mass transfer limitations on the reaction system. The analytical results are complemented by numerical simulations of the reaction-diffusion system based on the Gillespie algorithm.[34–37]

II. REACTION-DIFFUSION MASTER EQUATION AND CONCENTRATION PDF

We adopt here the population dynamics approach as proposed by Lugo and McKane.[32] The one-dimensional spatial domain is discretized into Ω cells of length h, each of which is assumed to be well-mixed.[24] For the well mixed condition to hold, the characteristic diffusion time over h is required to be less than the characteristic reaction time,[24] this means, $\tau_D = h^2/(2D) \leq \tau_k = 1/(\phi_0 k)$ with ϕ_0 is a characteristic species concentration. Notice that more precise criteria can be defined depending on the chemical reaction under consideration.[25, 26]

We impose periodic boundary conditions at the domain boundaries. In the adopted model, only particles that are in the same cell can react, and diffusion is modeled as a reaction between a particle in one cell and an empty space in a neighboring cell. Considering empty spaces, or holes, as virtual particles, diffusion processes are modeled as the exchange between a real particle in a cell and a hole in a nearest neighbor cell.[32]

The maximum occupation number of a cell N is equal to the sum of particles and holes. The number of particles of species s in cell j is denoted by $n_s(j)$, the number of holes, or empty spaces by $n_E(j)$. The local concentration of species s is defined as $\rho_s(j) = n_s(j)/N$. It denotes the probability to find a particle of species s in cell j. The system size is given by ΩN, that is, the maximum number of chemical species that can be in the system. Only a single event can occur per step of the reaction-diffusion process. To each possible event (chemical and physical transitions of any of the particles) a waiting time is associated, which is exponentially distributed.[36, 37] The event with the shortest waiting time occurs during a step. The exponential waiting time distribution reflects the fact that the system is locally (within a cell) well mixed and thus a Markov system.

The evolution of the reaction-diffusion system is stochastic. The system state at a given time t is characterized by the random vector,

$$\boldsymbol{\rho}(t) = [\rho_A(1,t), \rho_B(1,t), \rho_C(1,t), \ldots, \rho_A(\Omega,t), \rho_B(\Omega,t),$$
$$\times \rho_C(\Omega,t)]^T, \quad (4)$$

of species concentrations in each cell. The superscript T denotes the transpose. The process $\boldsymbol{\rho}(t)$ is by definition a Markov process. Its realizations are characterized by series of reaction and diffusion waiting times and initial distributions of species concentrations. The joint concentration PDF is obtained by sampling concentration values in each cell from this process,

$$P(\boldsymbol{\rho}, t) = \lim_{R \to \infty} \frac{1}{R} \sum_{r=1}^{R} N \delta_{N\boldsymbol{\rho}, N\boldsymbol{\rho}^{(r)}(t)} \equiv \overline{\delta_N[\boldsymbol{\rho} - \boldsymbol{\rho}(t)]}, \quad (5)$$

in which R is the number of realizations, $\boldsymbol{\rho}^{(r)}(t)$ denotes the concentration vector in realization r. The Kronecker delta $\delta_{N\boldsymbol{\rho}, N\boldsymbol{\rho}(t)}$ is 1 if $\boldsymbol{\rho} = \boldsymbol{\rho}(t)$ and 0 otherwise. The distribution $\delta_N[\boldsymbol{\rho} - \boldsymbol{\rho}(t)] = N\delta_{N\boldsymbol{\rho}, N\boldsymbol{\rho}(t)}$ converges to the Dirac delta in the thermodynamic limit of $N \to \infty$. The overbar denotes the ensemble average. Note that we use the same letter for the stochastic process $\boldsymbol{\rho}(t)$ and the associated sampling vector $\boldsymbol{\rho} = [\rho_A(1), \ldots, \rho(\Omega)]^T$. The probability distribution function $P(\boldsymbol{\rho}, t)$ denotes the joint probability of the particle numbers of all species in all cells and thus encodes the full statistical information about the reaction-diffusion system. The

probability that the concentrations of all reacting species in all cells is in $[\boldsymbol{\rho}, \boldsymbol{\rho} + d\boldsymbol{\rho}]$ is given by $P(\boldsymbol{\rho}, t)d\boldsymbol{\rho}$.

The evolution of the joint concentration PDF $P(\boldsymbol{\rho}, t)$ can be described by the reaction-diffusion master equation,[34,35]

$$\frac{\partial P(\boldsymbol{\rho}, t)}{\partial t} = \sum_j [\epsilon_A^+(j)\epsilon_B^+(j)\epsilon_C^-(j) - 1]T_{AB}(j)P(\boldsymbol{\rho}, t)$$

$$+ \sum_{s[jj']} [\epsilon_s^+(j)\epsilon_s^-(j') - 1]T_s(j|j')P(\boldsymbol{\rho}, t). \quad (6)$$

The step operators are defined through their action on $P(\boldsymbol{\rho}, t)$ as

$$\epsilon_s^{\pm}(j)P[\rho_A(1), \ldots, \rho_s(j), \ldots, \rho_C(\Omega), t]$$
$$= P[\rho_A(1), \ldots, \rho_s(j) \pm N^{-1}, \ldots, \rho_C(\omega), t]. \quad (7)$$

The notation $\sum_j$ indicates summation over all cells j and $\sum_{s[jj']}$ denotes summation over all species s and over all nearest neighbor pairs j and j'.

Following Refs. 27 and 32, we determine the transition probabilities per unit time from the mass action law, according to which the probability per time of a transition is proportional to the product of the concentrations of the two species that are involved in the chemical reaction or in the position exchange. The probability per time for a transition due to a reaction event in cell j, $T_{AB}(j)$, is given by

$$T_{AB}(j) = Nk\rho_A(j)\rho_B(j). \quad (8)$$

The rate constant k is assumed to be the same in all cells. The transition probability $T_s(j|j')$ for diffusion of a reactant particle of species s from cell j to the nearest neighbor cell j' is given by

$$T_s(j|j') = \frac{ND_s}{2h^2}\rho_s(j)\left[1 - \sum_m \rho_m(j')\right]. \quad (9)$$

The proportionality constant D_s ($s = A, B, C$) is assumed to be the same in all cells, but can vary between species. The system dynamics are fully defined by these transition probability rates. Note that the definition of the transition probability rates used here differs from the one employed in Lugo and McKane[32] by a factor of $N\Omega$. Using the definition of the transition rates given there,[27,32] requires rescaling of the rates *a posteriori*. For clarity, we did it *a priori*.

In the following, we will focus on the mean species concentrations defined by

$$\overline{\boldsymbol{\rho}}(t) = \lim_{R \to \infty} \frac{1}{R}\sum_{r=1}^R \boldsymbol{\rho}^{(r)}(t) = \int d\boldsymbol{\rho}\, \boldsymbol{\rho}\, P(\boldsymbol{\rho}, t). \quad (10)$$

Furthermore, we will illustrate the evolution of the concentration PDF by studying the PDF of concentration values of species s averaged over the whole domain, that is,

$$P_s(\rho, t) = \frac{1}{\Omega}\sum_{j=1}^{\Omega} \overline{\delta_N[\rho - \rho_s(j, t)]}. \quad (11)$$

The RDME (6) is solved numerically using the Gillespie algorithm,[36,37] which is modified to account for transitions between cells[27,32] as outlined above. The numerical simulations are performed in $R = 10^4$ realizations of the stochas-
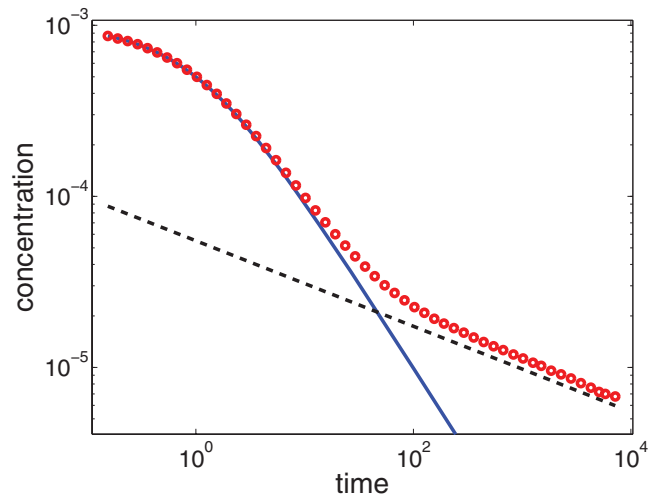

FIG. 1. Temporal behavior of the mean concentration of the A species. For early times the system follows the thermodynamic law, but for large times it deviates from t^{-1} to scale as $t^{-1/4}$. The blue solid line represents the slope t^{-1} and the black line $t^{-1/4}$. The red circles corresponds to results measured in simulations with the adopted model.

tic process. The maximum occupation number per cell is set to $N = 10^6$. The cell length is $h = 1$. The number of cells and thus the length of the spatial domain is $\Omega = 10^3$. In each realization, the initial concentrations $\rho_A(j, t_0)$ and $\rho_B(j, t_0)$ are chosen from independent Gaussian distributions with mean values $\overline{\rho}_A(j, t_0) = \overline{\rho}_B(j, t_0) = \rho_0 = 10^{-3}$ and variances $\sigma_{\rho_s}^2 = \overline{\rho}_s(j, t_0)/N = 10^{-9}$ for $s = A, B$. The concentration of species C is initially set to zero. The total number of particles at time t_0 is 10^5. Note that the Gaussian initial distribution of concentration values could, in principle, have unphysical negative values. For the setup used here, we did not record any negative concentrations. The diffusion rate constant is $D_s = 0.5$ for all species $s = A, B, C$ and the reaction rate constant is $k = D/\rho_0 = 5 \times 10^2$. As outlined above, the assumption that the cell is well-mixed requires that the characteristic diffusion time $\tau_D = h^2/(2D)$ is of the order of or smaller than the characteristic reaction time $\tau_k = 1/(k\rho_0)$. Figure 1 illustrates the behavior of the spatial average of the mean concentration of species A, $\|\overline{\rho(t)}_A\|$ defined as

$$\|\overline{\rho(t)}_A\| = \frac{1}{\Omega}\sum_{j=1}^{\Omega}\left[\frac{1}{R}\sum_{r=1}^R \rho_A^{(r)}(j, t)\right]. \quad (12)$$

At early times, the mean-field behavior t^{-1} is observed, as expected for the solution of a diffusive-reactive system under well-mixed conditions.[3] For larger times, when $\|\overline{\rho(t)}_A\|$ is of the order of the fluctuations, the spatial average of the mean concentration scales as $t^{-1/4}$, as observed by.[1–3] The crossover time can be obtained by equating the mean field behavior $1/(k\rho_0 t)$ and the anomalous $\sqrt{\rho_0}(Dt)^{-1/4}$ behavior derived by Ref. 3. Using $k = D/\rho_0$ as indicated above, one obtains for the crossover time t_c the scaling $t_c \propto \rho_0^{-2/3}$. When one of the two reactants is locally consumed, the reaction stops until diffusion mixes the reactants again and allow for further reactions to take place. Figure 2 shows the evolution of the concentration PDF with time. For small times, the concentration PDF
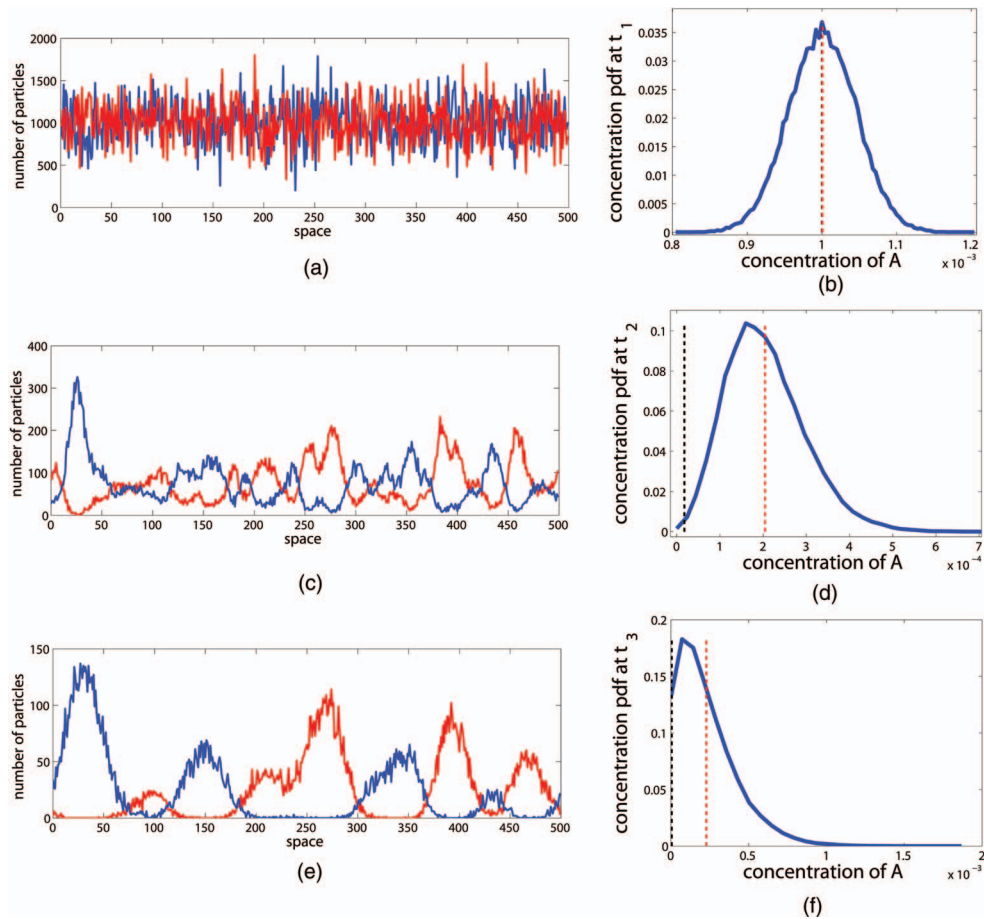
FIG. 2. Spatial distribution of particles in a single realization, (a), (c), and (e), and the ensemble probability density function $P_A(\rho, t)$ of concentration of species A averaged over the domain, see Eq. (11), (b), (d) and (f) at three times: $t_1 = 0$, $t_2 = 55.7$, and $t_3 = 178.7$ in arbitrary time units. On the right, the dashed vertical black line represents the mean field $\phi_A(t)$, and the red dashed vertical line represents the mean $\|\overline{\rho(t)}_A\|$ of the distribution $P_A(\rho, t)$. For $P_A(\rho, t)$ symmetric, the two values coincide. When $P_A(\rho, t)$ starts to become skewed the ensemble average of the concentration becomes larger than the mean-field value. The blue and red solid lines in (a), (c), and (e) correspond to the number of A and B particles, respectively. The top, middle, and bottom rows correspond to the times t_1, t_2, and t_3, respectively. The late times t_2 and t_3 correspond to the situation where islands are formed.

maintains the Gaussian shape of the initial distribution. As the mean concentration decreases and changes its scaling to the anomalous $t^{-1/4}$ behavior, the PDF becomes asymmetric. This change towards an asymmetric shape is due to the emerging segregation regime described in the literature.[1–3] On physical grounds concentration must be positive. Thus, as the mean concentration decreases, negative deviations are more limited than positive fluctuations.

To quantify the evolution of this PDF, and subsequently the first moment of the fluctuation distribution as well as the mean concentration, we apply the van Kampen system size expansion[20,38] to the RDME (6).

III. VAN KAMPEN EXPANSION AND FOKKER-PLANK EQUATION WITH MOVING BOUNDARIES

The RDME (6) encodes both deterministic dynamics and fluctuations due to the intrinsic stochasticity of the system. In order to systematically analyze these two phenomena we proceed as proposed by van Kampen.[20,38] We decompose the system state $\rho_s(j, t)$ into its mean field $\phi_s(j, t)$ and stochastic fluctuations $\xi_s(j, t)$,

$$\rho_s(j, t) = \phi_s(j, t) + \frac{\xi_s(j, t)}{\sqrt{N}}. \qquad (13)$$

The deterministic mean-field concentration $\phi_s(j, t)$ is obtained in the thermodynamic limit of infinite system size, $\phi_s(j, t) = \lim_{N \to \infty} \rho_s(j, t)$. The ensemble average over the fluctuations $\xi_s(j, t)/\sqrt{N}$ goes to zero in the limit of infinite system size N. In the following we focus on the PDF of the fluctuations $\boldsymbol{\xi}(t)$, which is defined by $\Pi(\boldsymbol{\xi}, t) = \overline{\delta_{\boldsymbol{\xi}, \boldsymbol{\xi}(t)}}$. In terms of the concentration PDF $P(\boldsymbol{\rho}, t)$, it is obtained by variable transform as

$$\Pi(\boldsymbol{\xi}, t) = N^{-1/2} P[\phi_s(j, t) + N^{-1/2}\xi_s(j, t)]. \qquad (14)$$

The evolution equation for $\Pi(\boldsymbol{\xi}, t)$ is obtained from a van Kampen expansion of the RDME (6). In Appendix A we obtain, at first order, the classical reaction-diffusion equations (A8) for the mean field and the following Fokker-

Planck equation for the fluctuations, at second order

$$\frac{\partial \Pi(\boldsymbol{\xi}, t)}{\partial t} = -\nabla_{\boldsymbol{\xi}} \cdot [\mathcal{A}(t) \cdot \boldsymbol{\xi} \, \Pi(\boldsymbol{\xi}, \tau)]$$
$$+ \nabla_{\boldsymbol{\xi}} \cdot [\mathcal{B}(t) \cdot \nabla_{\boldsymbol{\xi}} \Pi(\boldsymbol{\xi}, \tau)]. \quad (15)$$

Matrices $\mathcal{A}(t)$ and $\mathcal{B}(t)$ are defined in Appendix A.

For changing system size N, numerical simulations show that the deviation from the t^{-1} law is an effect of order of $N^{-1/2}$. This implies that higher order terms in the van Kampen expansion are not needed to describe this phenomenon. Notice that this is different for well-mixed chemical systems in which higher order terms of the van Kampen expansion are generally needed.[8,39] Thus, for incompletely mixed systems for which diffusion is the limiting factor, anomalous kinetics effects may arise already as a second-order effect.

The solution of Eq. (15) with natural boundary conditions is a multi-variate Gaussian distribution. However, the concentration $\rho_s(j) = \phi_s(j) + \xi_s(j)/\sqrt{N}$ is positive; thus the support of $\boldsymbol{\xi}$ is bounded. This implies that the fluctuations $\xi_s(j)$ are within the subdomains

$$\Xi_{sj} = \{\xi_s(j) | -\sqrt{N}\phi_s(j) \le \xi_s(j) \le \sqrt{N}[1 - \phi_s(j)]\}, \quad (16)$$

in which $\Xi = \prod_{sj} \Xi_{sj}$ is the full domain of the fluctuations, see Appendix C. Here, we focus on dilute systems characterized by small particle numbers, for which the anomalous scaling of reaction kinetics arises. Therefore, the upper bound of Eq. (15) is never reached and the lower bound is shown here to be responsible for anomalous kinetics. The domain of fluctuations $\boldsymbol{\xi}$ is a hypercube and each component $\xi_s(j)$ is confined within a segment whose size varies over time. Thus, the fluctuation PDF $\Pi(\boldsymbol{\xi}, t)$ evolves according to the Fokker-Planck equation (15) with moving boundaries.[39] Fluctuations about the mean field can be characterized by the moments,

$$\overline{\Pi_{i=1}^{n} \xi_{s_i}(j_i)} = \int_{\Xi} d\boldsymbol{\xi} \, \Pi_{i=1}^{n} \xi_{s_i}(j_i) \Pi(\boldsymbol{\xi}, t). \quad (17)$$

An evolution equation for the first moment is obtained using Eqs. (15) and (17). In Appendix B, we derive

$$\frac{d\overline{\xi}_s(j)}{dt} = (\overline{\mathcal{A} \cdot \boldsymbol{\xi}})_s + S_s(j, t). \quad (18)$$

We identify the volume term $(\overline{\mathcal{A} \cdot \boldsymbol{\xi}})_s$ and the surface term $S_s(j, t)$, which is defined by

$$S_s(j, t) = \int_{\partial \Xi} d\mathbf{n}_s(j) \cdot [\mathcal{A}(t) \cdot \boldsymbol{\xi} \, \Pi(\boldsymbol{\xi}, \tau)]$$
$$+ \nabla_{\boldsymbol{\xi}} \cdot [\mathcal{B}(t) \cdot \nabla_{\boldsymbol{\xi}} \Pi(\boldsymbol{\xi}, \tau)]\xi_s(j), \quad (19)$$

where $\partial \Xi$ denotes the surface of the domain Ξ and $d\mathbf{n}_s(j)$ is the vector normal to the boundary surface. Physically, $\partial \Xi$ represents all possible states of the system given that at least one island is created, i.e., somewhere in the system at least one of the two species is absent and the chemical reaction stops locally. Note that for natural boundary conditions the surface terms are zero. As shown in Sec. II, at early times, when boundary effects play no role (i.e., no islands have formed), $\Pi(\boldsymbol{\xi}, t)$ can be approximated by a Gaussian with zero mean. With increasing time, the fluctuation PDF is growing more

and more skewed because the left boundary is approaching zero, see Eq. (16). Also note that the mean fluctuation is non-zero, see Figure 2, and the system behavior deviates from the mean field.

We now consider the mean concentration $\|\overline{\rho}_s\| = \frac{1}{\Omega} \sum_j \overline{\rho}_s(j, t)$, averaged over the spatial domain,

$$\|\overline{\rho}_s(t)\| = \|\phi_s(t)\| + \frac{\overline{\|\xi_s(t)\|}}{\sqrt{N}}. \quad (20)$$

At late times, $\|\phi_s(t)\|$ decreases as t^{-1}. Therefore, the scaling behavior $\|\overline{\rho}_s(t)\| \propto t^{-1/4}$ is governed by the mean fluctuation $\|\overline{\xi}_s(t)\|$. The scaling behavior of the latter can be obtained from the spatial average of Eq. (18). As outlined in Appendix A, to leading order, the space average of the volume term is zero. Thus, we obtain

$$\frac{d\|\overline{\xi}_s\|}{dt} = \|S_s(t)\|. \quad (21)$$

The surface term $\|S_s(t)\|$ controls the behavior of the mean fluctuation. Note that the surface of the fluctuation domain, $\partial \Xi$, corresponds to all possible fluctuation values when at least one island is formed, that is, when at least one species disappears locally. Mathematically this means that at least one of the lower subdomain boundaries, see Eq. (16), is reached, that is, $\xi_s(j) = -\sqrt{N}\phi_s(j)$.

In order to identify the scaling behavior of $\|\xi_s(t)\|$, we need to determine the surface term $\|S_s(t)\|$. The leading order contribution to $\|S_s(t)\|$ is given by

$$\|S_s(t)\| = \frac{1}{\Omega} \sum_j \sum_{s'j'} \int_{\partial \Xi_{sj'}} \xi_s(j) D_{s'} h^2 \xi_{s'}(j') \Pi(\boldsymbol{\xi}, t) d(\partial \Xi_{sj'}), \quad (22)$$

see Appendix A. Note that Eq. (22) represents a closure problem because the right side depends on the local values of $\xi_s(j)$. Here, we close the equation by evaluating the surface term numerically. We find that $\|S_s(t)\|$ scales as $t^{-5/4}$, see Figure 3. Direct integration of Eq. (21) shows that the mean fluctuation $\|\xi_s(t)\|$ scales as $t^{-1/4}$, which explains the scaling of the average concentration as $t^{-1/4}$, see Eq. (20).
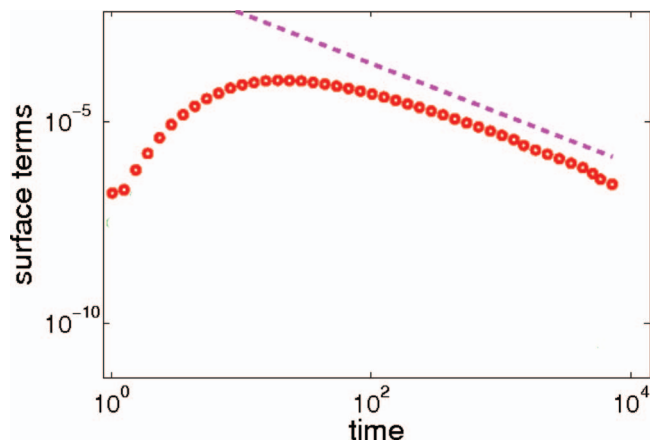

FIG. 3. The temporal behavior of the leading surface integral in Eq. (22) that describes the fluctuations. As expected it scales as $t^{-5/4}$. The red dots correspond to the numerical evaluation of this term with the adopted model. The magenta dashed line depicts a power law of $t^{-5/4}$.

IV. SUMMARY AND CONCLUSIONS

We study anomalous reaction kinetics that arise from the segregation of reactants in diffusion reaction systems. In the diffusion limited regime, islands containing a single reactant are created by self organization of the system. We adopt a stochastic approach based on the population dynamics and a numerical method based on a suitably modified Gillespie algorithm to study these dynamics. It is found that the breakdown of the mean field behavior and the transition to anomalous reaction scaling is related to the transition of the concentration PDF from a Gaussian to non-Gaussian shape.

At large time, the behavior of the reaction-diffusion system is dominated by the concentration fluctuations, whose impact on the reaction behavior can be quantified by its first moment, which, for finite system size, is different from zero. We apply the van Kampen system size expansion to the RDME. The first order of the expansion provides equations for the mean field. The second order provides a Fokker-Plank equation with moving boundaries for the PDF of the concentration fluctuations. The fluctuation domain is bounded because the concentration has non-negative values by definition. The lower limit is given in terms of the mean-field concentration, which decreases to zero as t^{-1}. At large mean concentrations, the lower boundary is negligible and the fluctuation PDF is close to a Gaussian with zero mean. As the mean-field concentration goes to zero, the fluctuation PDF deviates significantly from the Gaussian shape. In this regime, the mean concentration is dominated by the mean fluctuation, which is completely determined by the surface terms, Eq. (22), at the lower concentration boundary. These terms reflect the formation of islands. This result establishes a link between anomalous reaction kinetics and non-Gaussian concentration PDF.

APPENDIX A: THE VAN KAMPEN EXPANSION

Using relation (14) in Eq. (6), we obtain the following governing equation for $\Pi(\boldsymbol{\xi}, t)$:

$$\frac{\partial \Pi(\boldsymbol{\xi}, t)}{\partial t} - \sqrt{N} \frac{d\boldsymbol{\phi}}{dt} \cdot \nabla_{\boldsymbol{\xi}} \Pi(\boldsymbol{\xi}, t)$$

$$= \sum_j [\epsilon_A^+(j) \epsilon_B^+(j) \epsilon_C^-(j) - 1] T_{AB}(j) \Pi(\boldsymbol{\xi}, t)$$

$$+ \sum_{s[jj']} (\epsilon_s^+(j) \epsilon_s^-(j') - 1) T_s(j|j') \Pi(\boldsymbol{\xi}, t). \quad \text{(A1)}$$

For large N, the step operator (7) can be expanded in powers of $N^{-1/2}$ and expressed in differential form as[20, 38]

$$\epsilon_s^\pm(j) \Pi[\xi_A(1), \ldots, \xi_s(j), \ldots \xi_C(\Omega), t]$$

$$= \left[1 + \sum_{k=1}^\infty \frac{(\pm 1)^k}{k!} N^{-k/2} \frac{\partial^k}{\partial \xi_s(j)^k}\right] \Pi(\boldsymbol{\xi}, t). \quad \text{(A2)}$$

Inserting Eqs. (13) and (A2) into the right side of Eq. (A1) yields an expansion of the RDME in powers of $N^{-1/2}$. It has to be noticed that the transition probabilities are proportional to N.

The governing equations for the mean field $\phi_s(j, t)$ can be obtained from the leading order term of the van Kampen expansion. Expanding the right side of Eq. (A1) up to order $\sqrt{N}$, we obtain in leading order

$$\frac{d\boldsymbol{\phi}}{dt} \cdot \nabla_{\boldsymbol{\xi}} \Pi(\boldsymbol{\xi}, t) = (\boldsymbol{r} + \boldsymbol{D}) \cdot \nabla_{\boldsymbol{\xi}} \Pi(\boldsymbol{\xi}, t), \quad \text{(A3)}$$

where the vector $\boldsymbol{r}$ is defined by

$$r_s(j, t) = -k\phi_A(j, t)\phi_B(j, t), \quad r_C(j, t) = k\phi_A(j, t)\phi_B(j, t) \quad \text{(A4)}$$

for $s = A, B$. The vector $\boldsymbol{D}$ is given by

$$D_s(j, t) = D_s \left\{ \Delta\phi_s(j, t) \left[1 - \sum_m \phi_m(j, t)\right] \right.$$

$$\left. + \phi_s(j, t) \sum_m \Delta\phi_m(j, t) \right\}, \quad \text{(A5)}$$

in which we defined the discrete Laplacian $\Delta\phi_s(j, t) = h^{-2} \sum_{[j'|j]} [\phi_s(j', t) - \phi_s(j, t)]$; $\sum_{[j'|j]}$ denotes the sum over the nearest neighbors of j. Thus, we obtain for the mean field $\phi_s(j, t)$,

$$\frac{d\phi_s(j)}{dt} = D_s \left\{ \Delta\phi_s(j, t) \left[1 - \sum_m \phi_m(j, t)\right] \right.$$

$$\left. + \phi_s(j, t) \sum_m \Delta\phi_m(j, t) \right\} - k\phi_A(j, t)\phi_B(j, t), \quad \text{(A6)}$$

$$\frac{d\phi_C(j)}{dt} = D_C \left\{ \Delta\phi_C(j, t) \left[1 - \sum_m \phi_m(j, t)\right] \right.$$

$$\left. + \phi_C(j, t) \sum_m \Delta\phi_m(j, t) \right\} + k\phi_A(j, t)\phi_B(j, t), \quad \text{(A7)}$$

for $s = A, B$. In the spatial continuum limit for an observation scale $L \gg h$ and for dilute solutions, $\phi_s(j) \ll 1$, Eqs. (A6) and (A7) reduce to

$$\frac{\partial \phi_s(x, t)}{\partial t} = D_s \Delta\phi_A(x, t) - k\phi_A(x, t)\phi_B(x, t),$$

$$\frac{\partial \phi_C(x, t)}{\partial t} = D_C \Delta\phi_C(x, t) - k\phi_A(x, t)\phi_B(x, t). \quad \text{(A8)}$$

We identified here $\phi_s(j, t) = \phi_s(x, t)$. If the system is not dilute, Eqs. (A6) and (A7) do not reduce to the classical reaction-diffusion equations as discussed in Ref. 40.

The governing equation for the fluctuation PDF, $\Pi(\boldsymbol{\xi}, t)$ is obtained from the contributions to Eq. (A1) of the order one. Thus, we obtain

$$\frac{\partial \Pi(\boldsymbol{\xi}, t)}{\partial t} = (G_1 + R_1 + G_2 + R_2)\Pi(\boldsymbol{\xi}, t). \tag{A9}$$

The R_i ($i = 1, 2$) refers to terms that originate in the reactive transitions and are given by

$$R_1 = \sum_j \left\{ -\left[\frac{\partial}{\partial \xi_C(j)} - \frac{\partial}{\partial \xi_A(j)} - \frac{\partial}{\partial \xi_B(j)} \right] \right.$$
$$\left. \times\ k[\xi_A(j)\phi_B(j) + \xi_B(j)\phi_A(j)] \right\}, \tag{A10}$$

$$R_2 = \sum_j \left[\frac{\partial}{\partial \xi_C(j)} - \frac{\partial}{\partial \xi_A(j)} - \frac{\partial}{\partial \xi_B(j)} \right]^2 k\phi_A(j)\phi_B(j). \tag{A11}$$

The terms G_i ($i = 1, 2$) are due to the diffusion transitions. They read as

$$G_1 = -D_s \sum_{js} \frac{\partial}{\partial \xi_s(j)} \left[\Delta\xi_s(j) + \xi_s(j) \sum_m \Delta\phi_m(j) - \Delta\phi_s(j) \right.$$

$$\left. \times \sum_m \xi_m(j) + \phi_s(j) \sum_m \Delta\xi_m(j) - \Delta\xi_s(j) \sum_m \phi_m(j) \right], \tag{A12}$$

$$G_2 = \frac{D_s}{4} \sum_s \sum_{s[jj']} \left\{ \phi_s(j) \left[1 - \sum_m \phi_m(j') \right] \right.$$
$$+ \phi_s(j') \left[1 - \sum_m \phi_m(j) \right] \right\}$$
$$\times \left[\frac{\partial^2}{\partial \xi_s(j)^2} + \frac{\partial^2}{\partial \xi_s(j')^2} - 2\frac{\partial^2}{\partial \xi_s(j)\partial \xi_s(j')} \right]. \tag{A13}$$

From the analytical expressions obtained for R_1, R_2, G_1, and G_2, it is possible to express the sums as scalar product between the matrix $\mathcal{A}(t)$ and $\mathcal{B}(t)$ and the vector $\boldsymbol{\xi}$ of all the fluctuations. Doing this we can express Eq. (A9) as

$$\frac{\partial \Pi(\boldsymbol{\xi}, t)}{\partial t} = -\nabla_{\boldsymbol{\xi}} \cdot [\mathcal{A}(t) \cdot \boldsymbol{\xi}\, \Pi(\boldsymbol{\xi}, t)]$$
$$+ \nabla_{\boldsymbol{\xi}} \cdot [\mathcal{B}(t) \cdot \nabla_{\boldsymbol{\xi}}\, \Pi(\boldsymbol{\xi}, t)]. \tag{A14}$$

The latter is a linear multi-variate Fokker-Planck equation, where $\mathcal{A}(t)$ and $\mathcal{B}(t)$ are $3\Omega \times 3\Omega$ matrices that we can write as a $\Omega \times \Omega$ block matrices

$$\mathcal{A} = \begin{bmatrix} \mathcal{A}_0(1) & \mathcal{C}_1(2) & 0 & \ldots & \mathcal{C}_1(\Omega) \\ \mathcal{C}_1(1) & \mathcal{A}_0(2) & \mathcal{C}_1(3) & \ldots & 0 \\ \ldots & \ldots & \ldots & \ldots & \ldots \\ \mathcal{C}_1(1) & 0 & 0 & \ldots & \mathcal{A}_0(\Omega) \end{bmatrix} \text{ with blocks}$$

$$\mathcal{A}_0(j) = \begin{bmatrix} a_{AA}(j) & a_{AB}(j) & a_{AC}(j) \\ a_{BA}(j) & a_{BB}(j) & a_{BC}(j) \\ a_{CA}(j) & a_{CB}(j) & a_{CC}(j) \end{bmatrix}$$
$$\mathcal{C}_1(j') = \begin{bmatrix} c_{AA}(j') & c_{AB}(j') & c_{AC}(j') \\ c_{BA}(j') & c_{BB}(j') & c_{BC}(j') \\ c_{CA}(j') & c_{CB}(j') & c_{CC}(j') \end{bmatrix}, \tag{A15}$$

in which

$$a_{AA}(j) = -k\phi_B(j) + D_A h^2(2 - \sum_m \Delta\phi_m(j) - \Delta\phi_A(j)$$
$$+ 2\phi_A(j) - 2\sum_m \phi_m(j)), \tag{A16}$$

$$a_{AB}(j) = -k\phi_A(j) + D_A h^2(\Delta\phi_A(j) + 2\phi_A(j)), \tag{A17}$$

$$a_{AC}(j) = D_A h^2(\Delta\phi_A(j) + 2\phi_A(j)), \tag{A18}$$

$$a_{BA}(j) = -k\phi_B(j) + D_B h^2(\Delta\phi_B(j) + 2\phi_B(j)), \tag{A19}$$

$$a_{BB}(j) = -k\phi_A(j) + D_B h^2(2 - \sum_m \Delta\phi_m(j) - \Delta\phi_B(j)$$
$$+ 2\phi_B(j) - 2\sum_m \phi_m(j)), \tag{A20}$$

$$a_{BC}(j) = D_B h^2(\Delta\phi_B(j) + 2\phi_B(j)), \tag{A21}$$

$$a_{CA}(j) = k\phi_B(j) + D_C h^2(\Delta\phi_C(j) + 2\phi_C(j)), \tag{A22}$$

$$a_{CB}(j) = -k\phi_A(j) + D_C h^2(\Delta\phi_C(j) + 2\phi_C(j)), \tag{A23}$$

$$a_{CC}(j) = D_C h^2 \left(2 - \sum_m \Delta\phi_m(j) - \Delta\phi_C(j) \right.$$

$$\left. + 2\phi_C(j) - 2\sum_m \phi_m(j) \right), \qquad (A24)$$

$$c_{ss}(j') = -D_s h^2 (1 + \phi_s(j') - \sum_m \phi_m(j')), \quad (A25)$$

$$c_{sr}(j') = -D_s h^2 \phi_s(j'), \qquad (A26)$$

and

$$\mathcal{B} = \begin{bmatrix} \mathcal{B}_0(1) & \mathcal{D}_1(2) & 0 & \dots & \mathcal{D}_1(\Omega) \\ \mathcal{D}_1(1) & \mathcal{B}_0(2) & \mathcal{D}_1(3) & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots \\ \mathcal{D}_1(1) & 0 & 0 & \dots & \mathcal{B}_0(\Omega) \end{bmatrix} \quad \text{with blocks}$$

$$\mathcal{B}_0(j) = \begin{bmatrix} b_{AA}(j) & b_{AB}(j) & b_{AC}(j) \\ b_{BA}(j) & b_{BB}(j) & b_{BC}(j) \\ b_{CA}(j) & b_{CB}(j) & b_{CC}(j) \end{bmatrix},$$

$$\mathcal{D}_1(j) = \begin{bmatrix} d_{AA}(j) & 0 & 0 \\ 0 & d_{BB}(j) & 0 \\ 0 & 0 & d_{CC}(j) \end{bmatrix}, \qquad (A27)$$

where

$$b_{AA}(j) = k\phi_A(j)\phi_B(j) - \frac{D_s}{2}\left(\phi_A(j)\left(1 - \sum_m \phi_m(j')\right) \right.$$

$$\left. + \phi_A(j')\left(1 - \sum_m \phi_m(j)\right) \right), \qquad (A28)$$

$$b_{AB}(j) = k\phi_A(j)\phi_B(j), \qquad (A29)$$

$$b_{AC}(j) = -k\phi_A(j)\phi_B(j), \qquad (A30)$$

$$b_{BA}(j) = k\phi_A(j)\phi_B(j), \qquad (A31)$$

$$b_{BB}(j) = k\phi_A(j)\phi_B(j) - \frac{D_s}{2}\left(\phi_B(j)\left(1 - \sum_m \phi_m(j')\right) \right.$$

$$\left. + \phi_B(j')\left(1 - \sum_m \phi_m(j)\right) \right), \qquad (A32)$$

$$b_{BC}(j) = -k\phi_A(j)\phi_B(j), \qquad (A33)$$

$$b_{CA}(j) = -k\phi_A(j)\phi_B(j), \qquad (A34)$$

$$b_{CB}(j) = -k\phi_A(j)\phi_B(j), \qquad (A35)$$

$$b_{CC}(j) = k\phi_A(j)\phi_B(j) - \frac{D_s}{2}\left(\phi_C(j)\left(1 - \sum_m \phi_m(j')\right) \right.$$

$$\left. + \phi_s(j')\left(1 - \sum_m \phi_m(j)\right) \right), \qquad (A36)$$

$$d_{ss}(j) = -D_s \phi_s(j)\left(1 - \sum_m \phi_m(j')\right). \qquad (A37)$$

At large times we disregard contributions to matrices $\mathcal{A}$ and $\mathcal{B}$ that are of the order of t^{-1}, that is, the terms that are proportional to the mean field $\phi_{sj}(t)$ and powers thereof. In this approximation, the matrix $\mathcal{B}$ is zero and the only non-zero components of matrix $\mathcal{A}$ are

$$a_{AA}(j) = 2D_A h^2, \qquad (A38)$$

$$a_{BB}(j) = 2D_B h^2, \qquad (A39)$$

$$a_{CC}(j) = 2D_C h^2, \qquad (A40)$$

$$c_{ss}(j) = -D_s h^2. \qquad (A41)$$

Thus, matrix $\mathcal{A}$ reduces to the discrete Laplacian operator. Inserting this approximation into Eq. (18) and summing over j, the volume term on the right side is zero. Furthermore, inserting the approximations for $\mathcal{A}$ and $\mathcal{B}$ into Eq. (19) and summation over j directly gives Eq. (22).

APPENDIX B: FIRST MOMENT OF THE FLUCTUATIONS

To calculate the first moment of the sj-th component of the fluctuations, we multiply the Fokker-Planck equation by $\xi_s(j)$. Integrating over the fluctuations domain Ξ, we obtain

$$\int_\Xi \xi_s(j)\frac{\partial \Pi(\boldsymbol{\xi}, t)}{\partial t}d\boldsymbol{\xi} = -\int_\Xi \xi_s(j)(\nabla_{\boldsymbol{\xi}} \cdot [\mathcal{A} \cdot \boldsymbol{\xi}\Pi(\boldsymbol{\xi}, t)]$$

$$+ \nabla_{\boldsymbol{\xi}}[\mathcal{B} \cdot \nabla_{\boldsymbol{\xi}}\Pi(\boldsymbol{\xi}, t)])d\boldsymbol{\xi}. \qquad (B1)$$

We integrate this expression by parts, obtaining volume and surface terms. Using the Divergence theorem, we can evaluate the integrals of divergence over a domain as integrals of the argument of the divergence over the surface of the domain. Considering that the system is dilute, we assume that $\Pi(\boldsymbol{\xi}, t) = 0$ at the upper boundary (for $\boldsymbol{\xi} \to \sqrt{N}(1 - \boldsymbol{\phi})$) and we obtain,

$$\frac{d\overline{\xi_s}}{dt} = (\overline{\mathcal{A} \cdot \boldsymbol{\xi}})_s + \sum_{s'j'} \int_{\partial \Xi} [\xi_s(j) \mathcal{A}_{s'j's'j'} \xi_{s'}(j') \Pi(\boldsymbol{\xi}, t)] \cdot d\mathbf{n}$$

$$+ \frac{1}{2} \sum_{s'j'} \int_{\partial \Xi} [\xi_s(j) \mathcal{B} \cdot \nabla_{s'j'} \Pi(\boldsymbol{\xi}, t)] \cdot d\mathbf{n}$$

$$- \frac{1}{2} \sum_{s'j'} \sum_{s''j''} \int_{\Xi} \boldsymbol{e}_{sj} \cdot (\mathcal{B}^T \cdot \nabla_{s''j''}) \Pi(\boldsymbol{\xi}, t) d\boldsymbol{\xi}$$

$$- \sum_{s'j'} \int_{\partial \Xi} \xi_s(j) \partial_t \xi_{s'}(j') \partial_t \Pi(\boldsymbol{\xi}, t) \boldsymbol{e}_{s'j'} \cdot d\mathbf{n}, \quad (B2)$$

where $\partial \Xi$ is the surface of the domain Ξ, $d\mathbf{n}$ is the vector orthogonal to the surface $\partial \Xi$, and $\boldsymbol{e}_s$ is a vector with all components equal to zero except the sj-th component which is equal to one. This quantity derives from the integration of the term ∇_s. For compactness of notation in the previous expression, we denoted $f_s(j) = f_s$, $f_{s'}(j') = f_{s'}$, and $f_{s''}(j'') = f_{s''}$.

APPENDIX C: THE FOKKER-PLANK EQUATION IN THE NON-REACTIVE ISLANDS REGIME

The number of reactants is a positively defined quantity. Therefore the support of $\boldsymbol{\xi}$ is bounded, because $\rho_s(j) = \phi_s(j) + \xi_s(j)/\sqrt{N}$ is bounded between 0 and N. This implies that the fluctuations $\xi_s(j)$ are bounded in the subdomains

$$\Xi_s(j) = \{\xi_s(j) | - \sqrt{N}\phi_s(j) \le \xi_s(j) \le \sqrt{N}[1 - \phi_s(j)]\}, \quad (C1)$$

with $\Xi = \prod_{sj} \Xi_{sj}$. As such the domain of fluctuations $\boldsymbol{\xi}$ is a hypercube and each component of $\xi_s(j)$ is confined within a segment whose size varies over time. In Appendix A, we derived the Fokker-Planck equation for the evolution of $\Pi(\boldsymbol{\xi}, t)$. We specify zero flux of $\Pi(\boldsymbol{\xi}, t)$ at the boundaries of the 3Ω-dimensional domain Ξ. For an infinite fluctuation domain Ξ and natural boundary conditions for $\Pi(\boldsymbol{\xi}, t)$, the solution of Eq. (15) is a multi-variate Gaussian distribution.[20,41] In this approximation, the solution is fully characterized by its first and second moments. The boundary terms in Eq. (B2) are zero. The average fluctuations $\overline{\xi}_s(j)$ decrease exponentially with time. As long as the natural boundary conditions are a valid approximation, the average behavior of the whole system will not be affected by fluctuations. For situations in which the mean field is not very large compared with the size

of fluctuations, the approximation of infinite fluctuation domain is no longer reasonable and boundary effects arise.

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