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Restart Could Optimize the Probability of Success in a Bernoulli Trial

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The recently noticed ability of restart to reduce the expected completion time of first-passage processes allows appealing opportunities for performance improvement in a variety of settings. However, complex stochastic processes often exhibit several possible scenarios of completion which are not equally desirable in terms of efficiency. Here we show that restart may have profound consequences on the splitting probabilities of a Bernoulli-like first-passage process, i.e., of a process which can end with one of two outcomes. Particularly intriguing, in this respect, is the class of problems where a carefully adjusted restart mechanism maximizes the probability that the process will complete in a desired way. We reveal the universal aspects of this kind of optimal behavior by applying the general approach recently proposed for the problem of first-passage under restart.

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Stochastic processes subject to restart appear in many disciplines including physics, chemistry, biology, and computer science. Restart means a sudden interruption of a process followed by its starting anew. In some contexts, the restart is an integral part of a phenomenon under study (e.g., substrate unbinding in enzymatic reactions [1] and recovery of RNA polymerase from the backtracked state [2]), while in others it plays the role of an external control tool (e.g., reinitialization of a randomized computer algorithm [3,4] and reduction of growing tumor to its initial size by chemical treatment [5]).

A significant amount of research has been dedicated to the study of the effect of a restart on first-passage properties. The growth of interest in this problem was triggered by the surprising observation that a restart may significantly reduce the mean first-passage time (MFPT). In recent years, it has been demonstrated in a range of diverse examples that a carefully chosen restart rate can bring the MFPT to a minimum [6–14]. Along with the investigation of particular cases, we witness ongoing attempts to reveal the general principles allowing us to navigate in a vast space of first-passage problems under restart. A remarkable result of these attempts is the discovery of universality displayed by all optimally restarted processes [15–17].

To the best of our knowledge, the first-passage process under restart considered so far had only one way of completion. In particular, a diffusion mediated search with stochastic resetting to the initial position [6]—a classic example of a first-passage problem under restart—ends if and only if a searcher finds a target. However, real-life settings often offer a variety of possible ways in which stochastic process can be completed. Plurality of the process outcomes may arise from the competition among several different first-passage phenomena or due to multiple thresholds for one and the same first-passage mechanism. Assume, for instance, that a gambler stops playing after winning a certain amount of money or getting ruined, whichever happens first [18,19]. In many-target search problems and diffusion-limited reactions, different completion scenarios may correspond to the finding of different targets [20–29]. In search problems with time constraints, a search process can finish either by target detection or by searcher or target death [30–38]. When there are several competing paths of chemical reaction, an individual molecule may be converted into one product or another, depending on which path has been realized [39–41]. Similarly, a biopolymer molecule may fold along one of many possible pathways to one of multiple native states [42–47]. In evolutionary biology and ecology, one could ask if a population goes extinct before its size attains some threshold level [48,49]. Clearly, the immense set of possibilities is not limited to these few examples.

What happens when a first-passage process with several possible outcomes becomes subject to a restart? The main goal of this Letter is to draw attention to a previously unknown type of optimal behavior in first-passage phenomena: a carefully chosen rate of Poisson restart brings the probability of observing a particular completion scenario to a maximum (or minimum). In other words, we argue that a stochastic restart could optimize the so-called *splitting probabilities* [50,51]. The effect is first illustrated in a particular example, and after that, we apply a general framework recently proposed in Ref. [17] by Pal and Reuveni to gain a deeper insight. For the sake of simplicity, we focus on the case where the process has exactly two possible outcomes, but the analysis can be directly extended to a more general situation. We show that the optimality of splitting probabilities always entails an exact match between the unconditional and conditional mean completion times of the process. Looking for further generalization, we go beyond the assumption of a Poisson restart and demonstrate advantage of the deterministic restart strategy in terms of attaining the most pronounced extrema of splitting probabilities.

The key properties of a first passage under restart have originally been learned from the one dimensional diffusion process [6]. We will use the same exemplary case to demonstrate the ability of a restart to optimize the splitting probabilities. Specifically, let us consider a mortal Brownian searcher with the diffusion constant D and the mortality rate α that starts from the initial position $x_0 \geq 0$. The search process ends either when the searcher dies or when it finds the immobile target located at $x = 0$. It is shown in Ref. [32] (see also [37]) that target detection occurs with the probability $p = e^{-\sqrt{\alpha x_0^2/D}}$. Assume now that the process is stochastically restarted; i.e., the searcher is returned to its initial position x_0 at some constant rate r [52]. What is the detection probability p_r in the presence of a restart? The exact solution of the initial-boundary value problem for the probability density of the searcher's position yields (see Supplemental Material [53])

$$p_r = \frac{r+\alpha}{\alpha e^{\sqrt{(r+\alpha)/D}x_0} + r}. \tag{1}$$

Analyzing Eq. (1), one can readily see that if $\alpha \geq \alpha_0 = (z^*)^2 D/x_0^2$, where $z^* \approx 1.59362\ldots$ is the solution to $z/2 = 1 - e^{-z}$, then p_r monotonically decreases as r increases from zero to infinity. Otherwise, when $\alpha < \alpha_0$, the probability p_r takes its maximum at the nonvanishing restart rate $r_0 = \alpha_0 - \alpha$. In Fig. 1 we plot p_r as a function of r/α_0 for different α/α_0.

Let us give a qualitative explanation for the observed behavior of p_r. If α is large compared to D/x_0^2, then the typical size of the region explored by the searcher during its lifespan is less than the initial distance to the target, and thus, a nonvanishing restart inevitably leads to a reduction of the search efficiency. Otherwise, when α is small in comparison with D/x_0^2, the searcher lives long enough to be able to reach the target via a typical diffusive path, but it is also able to execute a distant excursion in empty areas of the search space. These excursions prolong the search process and typically end with searcher death. Then, the nonvanishing restart rate censors the fatal paths and increases chances to find the target. On the other hand, too large of a restart rate hinders target detection, since the searcher has less time between restarts to reach the origin under the same mortality rate. This is why a nonvanishing optimal restart rate r^* exists, which brings the probability that the searcher will find the target before dying to a maximum.

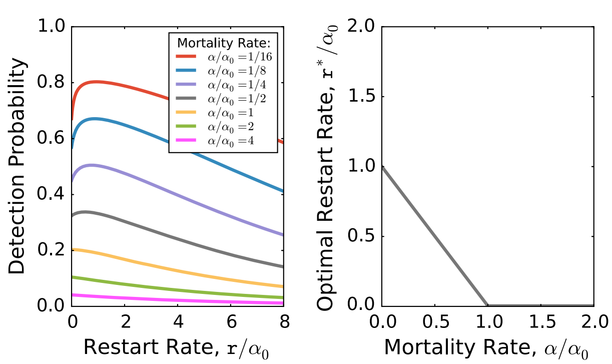

FIG. 1. (Left) The probability of target detection p_r versus the rate r of Poisson restart for different values of the searcher's decay constant α. (Right) Optimal restart rate as a function of the decay constant.

Having examined the exemplary case, we now turn to a more general setting. Let us consider a generic stochastic process that can end in two different ways and is subject to a generic restart mechanism. For the sake of convenience we will call one of the two possible outcomes "success" and the other "failure." Thus, the problem can be viewed as kind of a Bernoulli experiment, see Fig. 2(a). In the example discussed above, detection of the target naturally corresponds to success, while the searcher's death is interpreted as failure. Obviously, in other contexts, these conventional terms may not have any real meaning.

The original process is characterized by a random completion time T having the probability distribution $P(T)$. The later can be decomposed into a sum $P(T) = P^s(T) + P^f(T)$, where $P^s(T)$ and $P^f(T)$ are the probability densities of successful and failed trials, respectively. Normalization of the probability density $P^s(T)$ defines the "unperturbed" probability p of success: $p = \int_0^\infty P^s(T)dT$. We will also utilize the trivial fact that the ratio $P^s(T)/P(T)$ gives the probability of success in a trial with the completion time T [54].

Being subject to restart, the process can be interrupted at a random time R, characterized by a proper probability distribution $P^r(R)$, and started again. The probability p_r of success for the restarted process can be computed as the expectation of a binary random variable x, which takes the value 1 if the process is successfully completed and is equal

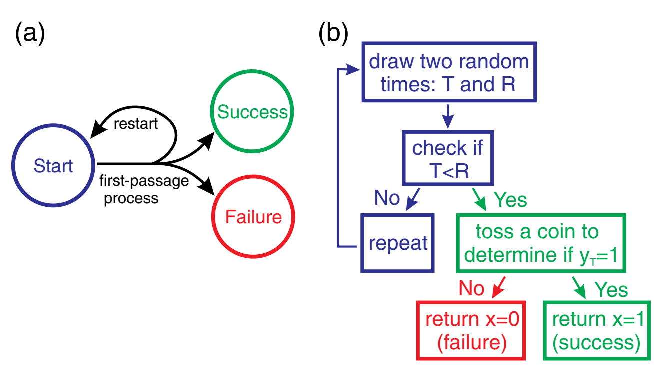

FIG. 2. (a) Bernoulli-like first-passage process under restart. (b) Pseudocode representation of Eq. (2).

to 0 in the case of failure. This variable obeys the following renewal equation:

$$x = I(T < R)y_T + I(T \geq R)x', \tag{2}$$

where $I(T < R) = 1 - I(T \geq R)$ is an indicator random variable that is equal to unity when $T < R$ and is zero otherwise; x' is an independent and identically distributed copy of x, and y_T is an auxiliary binary variable that takes the value one with the probability $P^s(T)/P(T)$.

The intuition behind Eq. (2) is very simple. Imagine that we run a computer simulation designed to reproduce behavior of the random variable x, see Fig. 2(b). At the first step, we should choose two random times from the distributions $P(T)$ and $P^r(R)$ and decide which of the two, restart or completion, happened first. If $T < R$, then the process is completed prior to restart. To determine whether the process ends in success or failure, we toss a coin with the probability of success $P^s(T)/P(T)$ and assign the outcome to the variable x. Otherwise, if $T \geq R$, the process begins completely anew, and we should repeat the procedure until the process reaches completion.

After averaging the statistics of the underlying process and random restart events, Eq. (2) yields

$$p_r = \langle x \rangle = \frac{\langle I(T < R)y_T \rangle}{\langle I(T < R) \rangle}. \tag{3}$$

Once the probability density functions $P^s(T)$ and $P^r(R)$ are known, one can readily compute $\langle I(T<R)y_T \rangle = \int_0^\infty \int_0^R P^r(R)P^s(T)dRdT$ and $\langle I(T < R) \rangle = \int_0^\infty \int_0^R P^r(R) P(T)dRdT$. When restart events come from Poisson statistics with a constant rate parameter r, the restart time R has an exponential distribution $P^r(R) = re^{-rR}$ and Eq. (3) reduces to

$$p_r = \frac{\tilde{P}^s(r)}{\tilde{P}(r)}, \tag{4}$$

where $\tilde{P}^s(r)$ and $\tilde{P}(r)$ denote the Laplace transforms of, respectively, $P^s(T)$ and $P(T)$ evaluated at r. Note that for the above problem of diffusion mediated search $P^s(T) = \sqrt{x_0^2/4\pi DT^3} e^{-\alpha T - x_0^2/4DT}$ and $P^f(T) = \alpha e^{-\alpha T} \mathrm{erf}(\sqrt{x_0^2/4DT})$ [37]. It is straight forward to show then that Eq. (4) reproduces Eq. (1) previously obtained through the less generic method (see SM [53]).

Noteworthy, at $r \to 0$, Eq. (4) yields $p_r \approx p + p(\langle T \rangle - \langle T^s \rangle)r$, where $\langle T \rangle = \int_0^\infty P(T)TdT$ and $\langle T^s \rangle = p^{-1} \int_0^\infty P^s(T)TdT$ represent, correspondingly, the unconditional MFPT of the original process and its MFPT conditional to success (assuming that these expectations as well as the high-order moments exist). Thus, the inequality $\langle T^s \rangle < \langle T \rangle$ gives a simple criteria of whether the introduction of a Poisson restart with an infinitesimally small rate will increase the success probability. In particular, for the mortal Brownian searcher we have $\langle T \rangle = (1 - e^{-\sqrt{x_0^2\alpha/D}})/\alpha$ and $\langle T^s \rangle = x_0/(2\sqrt{\alpha D})$ so that this criteria is satisfied only when $\alpha < \alpha_0$ in accord with the above analysis. Let us also stress that in some cases, applying restart at a high enough rate may be beneficial even when restart with a small rate decreases the chances of success. Indeed, one finds from Eq. (4) that at $r \to \infty$ the success probability becomes $p_r = \lim_{T\to 0} P^s(T)/P(T)$, and thus, it can take any value in the interval from zero to unity depending on the behavior of $P^s(T)$ and $P(T)$ at $T \to 0$.

We are mostly interested in the class of problems where the probability p_r is maximized for some optimal rate r^*. What do these problems all have in common? To address this question, let us take a look at the first-passage-time properties of the process illustrated in Fig. 2(a). As was shown in [17], the completion time T_r of a generic first-passage process under a generic restart mechanism obeys the following identity

$$T_r = I(T \geq R)(R + T_r') + I(T < R)T, \tag{5}$$

in which T_r' is an independent and identically distributed copy of T_r. Equation (5) allows one to express the MFPT as $\langle T_r \rangle = \langle \min(T, R) \rangle / \langle I(T < R) \rangle$, where $\min(T, R)$ is the minimum of T and R. Next, one could ask also how to compute the MFPT $\langle T_r^s \rangle$ conditional to success, which is simply the average completion time of successful trials. By virtue of its definition, this quantity can be written as $\langle T_r^s \rangle = \langle xT_r \rangle / \langle x \rangle$. Substituting Eqs. (2) and (5) into this relation results in

$$\langle T_r^s \rangle = \frac{\langle I(T > R)R \rangle}{\langle I(T < R) \rangle} + \frac{\langle I(T < R)y_T T \rangle}{\langle I(T < R)y_T \rangle}. \tag{6}$$

For an exponentially distributed restart, Eq. (6) takes a particularly simple form (see SM [53])

$$\langle T_r^s \rangle = \langle T_r \rangle - \frac{d \ln p_r}{dr}, \tag{7}$$

where p_r is given by Eq. (4) and $\langle T_r \rangle = r^{-1}(1 - \tilde{P}(r))/\tilde{P}(r)$ [16]. Equation (7) tells us that the response of the success probability to the change of the restart rate is determined by the difference between the unconditional and the conditional MFPTs; thus, generalizing the result of the asymptotic analysis. To demonstrate the general validity of Eq. (7), we numerically checked it in four different settings, see Fig. 3. Importantly, if the success probability p_r of the restarted process attains a maximum for some r^*, the second term in the right hand side of Eq. (7) vanishes and we get

$$\langle T_{r^*}^s \rangle = \langle T_{r^*} \rangle. \tag{8}$$

Also, since $p_r \langle T_r^s \rangle + (1 - p_r)\langle T_r^f \rangle = \langle T_r \rangle$, a similar identity holds true for the mean completion time of failed trials:

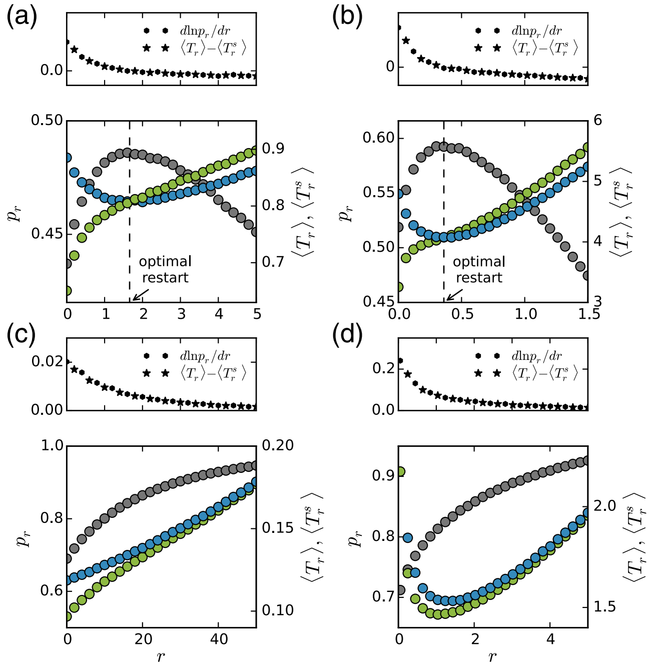

FIG. 3. The probability of success p_r (gray circles) and the MFPTs, $\langle T_r\rangle$ (blue circles) and $\langle T_r^s\rangle$ (green circles), versus the rate r of a Poisson restart obtained from the numerical simulations of a Bernoulli experiment in various settings: mortal Brownian searcher (a), mortal run-and-tumbling searcher (b), Brownian searcher and two competing targets (c), and two Brownian searchers competing for a target (d). As we see, the relation $(d\ln p_r/dr) = \langle T_r\rangle - \langle T_r^s\rangle$ [a simple rearrangement of Eq. (7)] is generally valid. The details of simulations can be found in [53].

$\langle T_{r^*}^f\rangle = \langle T_{r^*}\rangle$. We thus conclude that when the rate of a Poisson restart is optimal, in the sense that it maximizes or minimizes the probability to observe specific outcome, the unconditional MFPT is equal to the conditional MFPT in this outcome. This universal feature is shared by all optimally restarted processes irrespective on their fine details [see Figs. 3(a) and 3(b)].

The surprising simplicity of Eq. (8) calls for its intuitive explanation. To provide such an explanation, let us assume that one starts to observe a first-passage process, which is allowed to repeat itself over and over, at a random moment of time. What is then the *expected probability* $p^{\exp}$ of getting success in the next outcome? It can be shown that this probability is given by $p^{\exp} = p\langle T^s\rangle/\langle T\rangle$ (see SM [53]). Obviously, applying a Poisson restart with an infinitesimally small rate δr will increase the chances of success whenever $p^{\exp} < p$, while at $p^{\exp} > p$ the effect will be opposite. At the same time, if the process is already restarted at the optimal rate r^*, then $[dp_r/dr]_{r^*} = 0$ and a small additional correction δr to r^* does not change the probability of success p_{r^*} in the leading order approximation. Therefore, for the optimally restarted process, p_{r^*} must be equal to $p_{r^*}^{\exp} = p_{r^*}\langle T_{r^*}^s\rangle/\langle T_{r^*}\rangle$ that immediately leads to Eq. (8). Interestingly, the match of unconditional and conditional MFPTs is an inherent property of some two-thresholds first-passage processes relevant to kinetics of enzyme reactions [55,56], motor proteins dynamics [57], entropy-production fluctuations [58], and decision making [59]. For all these processes the splitting probabilities coincide with the corresponding expected splitting probabilities.

Anticipating that optimization is not an exclusive prerogative of a Poisson restart, it is natural to ask how to choose a restart time distribution $P^r(R)$ that provides the maximum probability of success p_r for a given first-passage process. Recently, it was proven that a deterministic restart [i.e., $P^r(R) = \delta(R - t)$] always outperforms stochastic restart strategies in terms of attaining the lowest MFPT [17]. Arguments similar to those used in [17] allow us to conclude that a deterministic restart is also universally preferable when one needs to optimize the splitting probabilities. It can be shown that if there exists such t^* that a deterministic restart with a restart time distribution $P^r(R) = \delta(R - t^*)$ brings the probability of success to a maximum p_{t^*}, then the value p_{t^*} cannot be exceeded by stochastic restart strategies (see SM [53]).

Equation (8) is no longer valid when restart events have non-Poisson statistics. Instead, the conditional and unconditional mean first-passage times of a process undergoing optimally tuned deterministic restart obey the universal inequality constraint

$$\langle T_{t^*}^s\rangle \geq \langle T_{t^*}\rangle. \tag{9}$$

To prove Eq. (9), let us assume that the process, which is being restarted deterministically in an optimal way, becomes subject to an additional Poisson restart with an infinitesimally small rate δr. That produces a deferential correction δp to the probability of success p_{t^*} attained by deterministic restart. Equation (7) allows us to write $\langle T_{t^*}\rangle - \langle T_{t^*}^s\rangle = \delta p/(p_{t^*}\delta r)$. Because of the dominance of a deterministic restart over other restart strategies, one can be sure that $\delta p \leq 0$, and therefore, $\langle T_{t^*}^s\rangle \geq \langle T_{t^*}\rangle$. Note also that the MFPT of failed trials satisfies the opposite inequality: $\langle T_{t^*}^f\rangle \leq \langle T_{t^*}\rangle$.

Conclusion.—When the different outcomes of a first-passage process are not equally valuable, the splitting probabilities may come to the fore as a crucial measure of efficiency and reliability [36–41,59] In this Letter, we applied a general theoretical approach to describe the effect of restart on the splitting probabilities of a process with exactly two possible completion scenarios. It was shown that a carefully chosen rate of Poisson restart could maximize (minimize) the probability that the process will complete in the desirable (undesirable) way. Whenever it is the case, the conditional and unconditional mean completion times are equal to each other. We also established the global dominance of a deterministic restart in the entire space of restart strategies—further evidence of the great optimization potential of deterministic restart in first-passage problems [12,17]. Note that these conclusions are robust to appearance of a generally distributed random time penalty for restart (see SM [53]). Thus, our work adds to the collection of universal results in the field of first-passage phenomena [16,17,60–63].

Of many implications of the above results, let us emphasize the issue relevant to chemical kinetics. The two fundamental problems of chemistry are control over the reaction rate [64] and the product selectivity [39–41]. As we know, thanks to the recent study of enzymatic reactions [1], the restart of a catalytic step can potentially accelerate the rate of product formation. The results of the present work lead to the complementary conclusion that when competing pathways of a chemical reaction end up with different products, the introduction of a restart mechanism may allow us to have control over the product ratio.

A particularly interesting line of future research concerns the so-called deadline meeting problem. As was noticed in computer science, a restart could help to increase the chances that a randomized search algorithm will find the solution before a prescribed deadline passes [65–67]. One could try to extend the analysis presented here to address the issue of universality of the optimal restart in this setting [68].

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[1] S. Reuveni, M. Urbakh, and J. Klafter, Role of substrate unbinding in Michaelis-Menten enzymatic reactions, Proc. Natl. Acad. Sci. U.S.A. **111**, 4391 (2014).

[2] É. Roldán, A. Lisica, D. Sánchez-Taltavull, and S. W. Grill, Stochastic resetting in backtrack recovery by RNA polymerases, Phys. Rev. E **93**, 062411 (2016).

[3] M. Luby, A. Sinclair, and D. Zuckerman, Optimal speedup of Las Vegas algorithms, Inf. Proc. Lett. **47**, 173 (1993).

[4] A. Montanari and R. Zecchina, Optimizing Searches Via Rare Events, Phys. Rev. Lett. **88**, 178701 (2002).

[5] S. Gupta, S. N. Majumdar, and G. Schehr, Fluctuating Interfaces Subject to Stochastic Resetting, Phys. Rev. Lett. **112**, 220601 (2014).

[6] M. R. Evans and S. N. Majumdar, Diffusion with Stochastic Resetting, Phys. Rev. Lett. **106**, 160601 (2011).

[7] M. R. Evans and S. N. Majumdar, Diffusion with optimal resetting, J. Phys. A **44**, 435001 (2011).

[8] J. Whitehouse, M. R. Evans, and S. N. Majumdar, Effect of partial absorption on diffusion with resetting, Phys. Rev. E **87**, 022118 (2013).

[9] M. R. Evans and S. N. Majumdar, Diffusion with resetting in arbitrary spatial dimension, J. Phys. A **47**, 285001 (2014).

[10] Ł. Kuśmierz, S. N. Majumdar, S. Sabhapandit, and G. Schehr, First Order Transition for the Optimal Search Time of Lévy Flights with Resetting, Phys. Rev. Lett. **113**, 220602 (2014).

[11] Ł. Kuśmierz and E. Gudowska-Nowak, Optimal first-arrival times in Lévy flights with resetting, Phys. Rev. E **92**, 052127 (2015).

[12] A. Pal, A. Kundu, and M. R. Evans, Diffusion under time-dependent resetting, J. Phys. A **49**, 225001 (2016).

[13] S. Eule and J. J. Metzger, Non-equilibrium steady states of stochastic processes with intermittent resetting, New J. Phys. **18**, 033006 (2016).

[14] A. Nagar and S. Gupta, Diffusion with stochastic resetting at power-law times, Phys. Rev. E **93**, 060102 (2016).

[15] T. Rotbart, S. Reuveni, and M. Urbakh, Michaelis-Menten reaction scheme as a unified approach towards the optimal restart problem, Phys. Rev. E **92**, 060101 (2015).

[16] S. Reuveni, Optimal Stochastic Restart Renders Fluctuations in First Passage Times Universal, Phys. Rev. Lett. **116**, 170601 (2016).

[17] A. Pal and S. Reuveni, First Passage Under Restart, Phys. Rev. Lett. **118**, 030603 (2017).

[18] A. W. F. Edwards, Pascal's problem: The Gambler's Ruin, Int. Stat. Rev. **51**, 73 (1983).

[19] W. Feller, *An Introduction to Probability Theory and Its Applications*, 3rd ed. (Wiley, New York, 1968), Vol. I.

[20] S. Condamin, O. Bénichou, and M. Moreau, Random walks and Brownian motion: A method of computation for first-passage times and related quantities in confined geometries, Phys. Rev. E **75**, 021111 (2007).

[21] S. Condamin, V. Tejedor, and O. Bénichou, Occupation times of random walks in confined geometries: From random trap model to diffusion-limited reactions, Phys. Rev. E **76**, 050102 (2007).

[22] S. Condamin, V. Tejedor, R. Voituriez, O. Bénichou, and J. Klafter, Probing microscopic origins of confined subdiffusion by first-passage observables, Proc. Natl. Acad. Sci. U.S.A. **105**, 5675 (2008).

[23] B. Meyer, E. Agliari, O. Bénichou, and R. Voituriez, Exact calculations of first-passage quantities on recursive networks, Phys. Rev. E **85**, 026113 (2012).

[24] T. Calandre, O. Bénichou, D. S. Grebenkov, and R. Voituriez, Interfacial territory covered by surface-mediated diffusion, Phys. Rev. E **85**, 051111 (2012).

[25] T. Calandre, O. Bénichou, D. S. Grebenkov, and R. Voituriez, Splitting probabilities and interfacial territory covered by two-dimensional and three-dimensional surface-mediated diffusion, Phys. Rev. E **89**, 012149 (2014).

[26] O. Bénichou, T. Guérin, and R. Voituriez, Mean first-passage times in confined media: from Markovian to non-Markovian processes, J. Phys. A **48**, 163001 (2015).

[27] G. Cencetti, F. Bagnoli, F. Di Patti, and D. Fanelli, The second will be first: competition on directed networks, Sci. Rep. **6**, 27116 (2016).

[28] P. L. Krapivsky and S. Redner, Trapping and escape in a turbid medium, J. Chem. Phys. **147**, 214903 (2017).

[29] U. Dobramysl and D. Holcman, Mixed analytical-stochastic simulation method for the recovery of a Brownian gradient source from probability fluxes to small windows, J. Comput. Phys. **355**, 22 (2018).

[30] I. Lohmar and J. Krug, Diffusion-limited reactions and mortal random walkers in confined geometries, J. Stat. Phys. **134**, 307 (2009).

[31] E. Abad, S. B. Yuste, and K. Lindenberg, Survival probability of an immobile target in a sea of evanescent diffusive or subdiffusive traps: A fractional equation approach, Phys. Rev. E **86**, 061120 (2012).

[32] E. Abad, S. B. Yuste, and K. Lindenberg, Elucidating the role of subdiffusion and evanescence in the target problem: Some recent results, Math. Model. Nat. Phenom. **8**, 100 (2013).

[33] S. B. Yuste, E. Abad, and K. Lindenberg, Exploration and Trapping of Mortal Random Walkers, Phys. Rev. Lett. **110**, 220603 (2013).

[34] E. Abad, S. B. Yuste, and K. Lindenberg, Evanescent continuous-time random walks, Phys. Rev. E **88**, 062110 (2013).

[35] E. Abad and J. J. Kozak, Competing reaction processes on a lattice as a paradigm for catalyst deactivation, Phys. Rev. E **91**, 022106 (2015).

[36] D. Campos, E. Abad, V. Méndez, S. B. Yuste, and K. Lindenberg, Optimal search strategies of space-time coupled random walkers with finite lifetimes, Phys. Rev. E **91**, 052115 (2015).

[37] B. Meerson and S. Redner, Mortality, Redundancy, and Diversity in Stochastic Search, Phys. Rev. Lett. **114**, 198101 (2015).

[38] D. S. Grebenkov and J. F. Rupprecht, The escape problem for mortal walkers, J. Chem. Phys. **146**, 084106 (2017).

[39] J. Rehbein and B. K. Carpenter, Do we fully understand what controls chemical selectivity?, Phys. Chem. Chem. Phys. **13**, 20906 (2011).

[40] J. Rehbein and B. Wulff, Chemistry in motion—off the MEP, Tetrahedron Lett. **56**, 6931 (2015).

[41] A. Martn-Sómer, M. Yáñez, W. L. Hase, M. P. Gaigeot, and R. Spezia, Post-Transition State Dynamics in Gas Phase Reactivity: Importance of Bifurcations and Rotational Activation, J. Chem. Theory Comput. **12**, 974 (2016).

[42] S. V. Solomatin, M. Greenfeld, S. Chu, and D. Herschlag, Multiple native states reveal persistent ruggedness of an RNA folding landscape, Nature (London) **463**, 681 (2010).

[43] M. S. Marek, A. Johnson-Buck, and N. G. Walter, The shape-shifting quasispecies of RNA: one sequence, many functional folds, Phys. Chem. Chem. Phys. **13**, 11524 (2011).

[44] C. Hyeon, J. Lee, J. Yoon, S. Hohng, and D. Thirumalai, Hidden complexity in the isomerization dynamics of Holliday junctions, Nat. Chem. **4**, 907 (2012).

[45] B. P. Paudel and D. Rueda, Molecular crowding accelerates ribozyme docking and catalysis, J. Am. Chem. Soc. **136**, 16700 (2014).

[46] M. Hinczewski, C. Hyeon, and D. Thirumalai, Directly measuring single-molecule heterogeneity using force spectroscopy, Proc. Natl. Acad. Sci. U.S.A. **113**, E3852 (2016).

[47] C. A. Pierse and O. K. Dudko, Distinguishing Signatures of Multipathway Conformational Transitions, Phys. Rev. Lett. **118**, 088101 (2017).

[48] R. Lande, S. Engen, and B. E. Saether, *Stochastic Population Dynamics in Ecology and Conservation* (Oxford University Press, New York, 2003).

[49] J. M. Drake and B. D. Griffen, Speed of expansion and extinction in experimental populations, Ecol. Lett. **12**, 772 (2009).

[50] N. V. Kampen, *Stochastic Processes in Physics and Chemistry* (North-Holland, Amsterdam, 1992).

[51] S. Redner, *A Guide to First-Passage Processes* (Cambridge University Press, Cambridge, 2001).

[52] Strictly speaking, we imply not only a resetting of the searcher's coordinate, but also a restart of the mortality mechanism. This remark is not essential in this particular example, where the searcher has the constant mortality rate α, which does not depend on the time elapsed since the previous restart (or start) event.

[53] See Supplemental Material at http://link.aps.org/supplemental/10.1103/PhysRevLett.120.080601, which includes Ref. [15] and Ref. [26], for derivations of Eqs. (1) and (7), a derivation of the expected probability of success, proof of the superiority of deterministic restart, a generalization of analysis that accounts random time penalty for restart, and details of numerical simulations.

[54] Clearly, $P^i(T)$, where i is either "s" (success) or "f" (failure), represents the joint probability distribution of the process outcome and completion time, while $p(s|T) = P^s(T)/P(T)$ is the conditional probability of success given the completion time T.

[55] H. Qian and X. S. Xie, Generalized Haldane equation and fluctuation theorem in the steady-state cycle kinetics of single enzymes, Phys. Rev. E **74**, 010902 (2006).

[56] H. Ge, Waiting cycle times and generalized Haldane equality in the steady-state cycle kinetics of single enzymes, J. Phys. Chem. B **112**, 61 (2008).

[57] A. B. Kolomeisky, E. B. Stukalin, and A. A. Popov, Understanding mechanochemical coupling in kinesins using first-passage-time processes, Phys. Rev. E **71**, 031902 (2005).

[58] I. Neri, É. Roldán, and F. Julicher, Statistics of Infima and Stopping Times of Entropy Production and Applications to Active Molecular Processes, Phys. Rev. X **7**, 011019 (2017).

[59] É. Roldán, I. Neri, M. Dörpinghaus, H. Meyr, and F. Jülicher, Decision Making in the Arrow of Time, Phys. Rev. Lett. **115**, 250602 (2015).

[60] S. Condamin, O. Bénichou, V. Tejedor, R. Voituriez, and J. Klafter, First-passage times in complex scale-invariant media, Nature (London) **450**, 77 (2007).

[61] O. Bénichou, C. Chevalier, J. Klafter, B. Meyer, and R. Voituriez, Geometry-controlled kinetics, Nat. Chem. **2**, 472 (2010).

[62] M. Chupeau, O. Bénichou, and R. Voituriez, Cover times of random searches, Nat. Phys. **11**, 844 (2015).

[63] D. S. Grebenkov, Universal Formula for the Mean First Passage Time in Planar Domains, Phys. Rev. Lett. **117**, 260201 (2016).

[64] P. Hanggi, P. Talkner, and M. Borkovec, Reaction-rate theory: fifty years after Kramers, Rev. Mod. Phys. **62**, 251 (1990).

[65] A. P. van Moorsel and K. Wolter, in Meeting Deadlines through Restart, in *MMB & PGTS 2004* (VDE, Verlag, 2004) p. 155160.

[66] H. Wu, Master's thesis, University of Waterloo, 2006.

[67] J. H. Lorenz, Completion Probabilities and Parallel Restart Strategies under an Imposed Deadline, PLoS One **11**, e0164605 (2016).

[68] The deadline meeting problem can be viewed as a competition between two first-passage processes, one of which can be controlled by applying a restart, while the progress of another (deadline mechanism) is uncontrolled.