We derive a thermodynamic uncertainty relation (TUR) for first-passage times (FPTs) on continuous time Markov chains. The TUR utilizes the entropy production coming from bidirectional transitions, and the net flux coming from unidirectional transitions, to provide a lower bound on FPT fluctuations. As every bidirectional transition can also be seen as a pair of separate unidirectional ones, our approach typically yields an ensemble of TURs. The tightest bound on FPT fluctuations can then be obtained from this ensemble by a simple and physically motivated optimization procedure. The results presented herein are valid for arbitrary initial conditions, out-of-equilibrium dynamics, and are therefore well suited to describe the inherently irreversible first-passage event. They can thus be readily applied to a myriad of first-passage problems that arise across a wide range of disciplines.

Many interesting phenomena occurring at the molecular scale can be viewed as first-passage processes [1]. From chemical reactions [2–6] to enzyme catalysis [7–13] and molecular search processes [14–18] — one is interested in the exact moment at which a distinguished event occurs: the first passage time (FPT) [1, 19–21]. Thermal agitations make FPTs random and much effort has been directed to determining their governing statistics in theory and experiment [22–27]. Of particular interest in that regard is the relative magnitude of FPT fluctuations around their mean value. This central gauge of randomness has found numerous uses and applications [6, 11–13, 18, 23–26, 28–38]. Yet, owing to conceptual and technical challenges, its relation with the underlying thermodynamics remains poorly understood.

The first passage event is often described as a completely irreversible step, and as a result such processes are inherently out-of-equilibrium. The theory of stochastic thermodynamics was developed to describe the nonequilibrium thermodynamics of small stochastic systems, such as molecular motors, enzymes, and nanomachines [39–45]. One of the celebrated results in the field is the thermodynamic uncertainty relation (TUR) [46, 47]. First conjectured by Barato and Seifert, the TUR states that the normalized fluctuations of currents are bounded from below by the inverse entropy production. The fundamental nature of the TUR has spurred an intensive research effort [48–61].

There has only been a handful attempts to extend the TUR to FPTs. Garrahan [62], whose work was later on generalized by Gingrich and Horowitz [63], derived a TUR for a fluctuating current that crosses a predetermined threshold for the first time. More recently, Falasco and Esposito have derived a dissipation based speed limit on the mean arrival time to a target [64]. Notably all the above-mentioned works focus on systems in steady state. In contrast, in first-passage processes, such as the one depicted in Fig. 1, one is primarily interested in the transient dynamics. Moreover, the transition to the absorbing state is irreversible and therefore its entropy production is ill defined. These conceptual issues make an extension of the TUR to FPT processes both interesting and challenging.

In this letter, we derive a TUR for the first-passage time to a site on a Markov chain. The result is derived from a more general set up that we have recently introduced to study systems with unidirectional transitions [59]. Like other TURs, the TUR derived herein bounds the relative fluctuations of the first-passage time, but its validity is not limited by the steady-state assumption and it can moreover be applied directly to systems with absorbing states. As this manuscript was being prepared Hiura and Sasa presented a kinetic TUR for first passage times [65] (see also [66, 67] for other kinetic TURs for currents). At the end of this letter, we show that the TUR derived in [65] follows from ours as a special case.

First passage on a continuous time Markov chain. — On a Markov network, the probability to find the system in different states evolves according to the master
where \( \tau \) is the transition rates matrix. Its off diagonal

\[
\Gamma = \begin{bmatrix}
\Gamma & 0 \\
K_{\text{out}} & 0
\end{bmatrix}
\]

where \( \Gamma \) accounts for the transitions between the regular states. \( K_{\text{out}} = (K_{N+1,1}, K_{N+1,2}, \ldots, K_{N+1,N}) \) is a row

vector containing the transition rates to the absorbing state. For this class of models the distribution of first passage times is given by

\[
\rho(\omega) = \Gamma \rho(\omega) ,
\]

where \( \rho(\omega) = (\rho_0(\omega), \rho_1(\omega), \ldots, \rho_N(\omega)) \) is a vector containing the transition rates to the absorbing state. For this class of models the distribution of first passage times is given by

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\[
\rho(\omega) = \Gamma \rho(\omega) ,
\]
Using $\int_0^T dt \ S(t) = \mathcal{T}\ S(T) + \int_0^T dt \ f_T(t)$ and $\langle T \rangle = \lim_{T \to \infty} \int_0^T dt \ f_T(t)$, we recast Eq. (5) as

$$CV^2 \geq \frac{1}{\int_0^\infty dt \ \left[ \frac{1}{2} \sigma_{rev}(t) + J_{uni}(t) \right]}.$$  \hspace{1cm} (8)

Eq. (8) is the central result of this paper. It shows that the coefficient of variation of the first passage time is bounded from below by an expression that combines the entropy production from the transitions in $E_2$ and the fluxes from the transitions in $E_1$. We now discuss different representations of the bound that arise from the freedom to place transitions in either of these groups.

Entropic bound.— This form of the bound is obtained when all the bidirectional transitions are treated as such and put in group $E_2$. The remaining transitions are thus those that lead to the absorbing site $A$. Given that the system is initially distributed somewhere among the sites $i \neq A$, and that $P_A(t \to \infty) = 1$, one finds that

$$\int_0^\infty dt J_{uni}(t) = \int_0^\infty dt P_A(t) = P_A(\infty) - P_A(0) = 1.$$ \hspace{1cm} (9)

The entropy production from all other transitions is given by

$$\Sigma_{rev} = \frac{1}{2} \sum_{(j \to i) \in E_2} \int_0^\infty dt [K_{ij} P_j(t) - K_{ji} P_i(t)] \ln \frac{K_{ij} P_j(t)}{K_{ji} P_i(t)}.$$ \hspace{1cm} (10)

The entropic version of the bound is then given by

$$CV^2 \geq \frac{1}{\Sigma_{rev} + 1}. \hspace{1cm} (11)$$

Kinetic bound.— The kinetic bound is obtained when all the reversible transitions, that were placed in $E_2$ in the entropic form of the bound, are treated as pairs of irreversible transitions and put in $E_1$. As a result, the reversible entropy production vanishes. In contrast, $\Sigma_{uni}$ is the integrated flux from all transitions, namely,

$$\Sigma_{uni} = \int_0^\infty dt J_{uni}(t) = \sum_{(j \to i)} \int_0^\infty dt K_{ij} P_j(t).$$ \hspace{1cm} (12)

In this case one obtains the bound

$$CV^2 \geq \frac{1}{\Sigma_{uni}}.$$ \hspace{1cm} (13)

Mixed bounds.— Clearly Eqs. (11) and (13) follow extreme cases in which one considers the maximally possible number of transitions to be either bidirectional or unidirectional. Yet, one may also utilize the freedom to place some bidirectional transitions in $E_2$, while treating others as pairs of unidirectional directional transitions to be placed in $E_1$. This leads to a bound of the form

$$CV^2 \geq \frac{1}{\frac{1}{2} \Sigma_{rev} + \Sigma_{uni}}.$$ \hspace{1cm} (14)

Here $\Sigma_{rev}$ and $\Sigma_{uni}$ are similar to (10) and (12), but with the summation restricted to the appropriate subset of transitions.

The optimal bound.— The validity of several bounds raises a natural question: which bound should one use? We argue that the tightest bound is typically the most useful one. A simple algorithm allows to obtain the best bound from the family of bounds considered here. One has to scan over all pairs of sites $i, j$. For every pair of transitions $i \to j$ and $j \to i$ that can belong either to $E_1$ or to $E_2$ one calculates the quantities $\Sigma_1 = \int_0^\infty dt [K_{ij} P_j(t) + K_{ji} P_i(t)]$ and $\Sigma_2 = \int_0^\infty dt [K_{ij} P_j(t) - K_{ji} P_i(t)] \ln \frac{K_{ij} P_j(t)}{K_{ji} P_i(t)}$. If $\Sigma_1 < \Sigma_2$ one includes a contribution of $\Sigma_1$ in $\Sigma_{uni}$. Alternatively, one includes a contribution of $\Sigma_2$ in $\Sigma_{rev}$.

We call this bound the optimal bound, where the term optimal refers to the optimal partition of transitions into $E_1$ and $E_2$. Finding this optimal partition is relatively easy since each transition can be treated separately. Moreover, in many cases one can use physical intuition to figure out what to do with a given transition. For example, if a transition is expected to be almost detailed balanced, $K_{ij} P_j(t) \simeq K_{ji} P_i(t)$, then it is highly likely that $\Sigma_2 < \Sigma_1$ as illustrated below. An illustrative example.— A simple model of a one dimensional random walker is used to elucidate our approach and to connect to related results. The model consists of a linear chain of six sites, where the leftmost site is reflecting and the rightmost is absorbing [Fig. 2(a)]. The walker starts at the leftmost site, and jumps from site to site. All forward transitions in the model occur with rate $k_+$, except the $3 \to 4$ and $5 \to 6$ transitions that occur with rates $k_+$ and $k_f$ respectively. All backward transitions in the model occur with rate $k_-$, except the $4 \to 3$ transition that occurs with rate $k_l$. This parameterization of rates is flexible enough to exhibit several types of physically interesting behaviour.

In Fig. 2(b), we demonstrate that the optimal bound transitions from the entropic form of Eq. (11) to the kinetic form of Eq. (13). To do so we set $k_+ = k_+ = k_f = 1$, and $k_- = k_l = e^{-\epsilon}$; and observe that all transitions are approximately unidirectional when $\epsilon$ is large. In this limit entropy production is very high. It is thus no surprise that replacing entropic with kinetic terms results in a tighter bound. On the other extreme, for small values of $\epsilon$, there is almost no bias which results in a quasi-equilibrium on the bulk of the lattice as probability gradually leaks to the absorbing site. In this limit, entropy production is much lower and the inclusion of entropic terms leads to tighter bound. (We use the term quasi-equilibrium loosely, as the flux to the absorbing site is not small.) For intermediate values of $\epsilon$, there is a crossover region where the behaviour is more complex leading to a mixed optimal bound that includes both entropic and kinetic terms (Fig. 2(b) inset).
To show that a mixed bound can be optimal in large regions of the phase space, we make a different choice for the rates in Fig. 2(a): $k_+ = k_- = 1$, $k_r = k_f = 1/3$, and $k_l = e^{-\epsilon}/5$. The lattice is then approximately divided into two blocks: that of sites \{1, 2, 3\} and that of sites \{4, 5\}, with less frequent transitions between the blocks. When $\epsilon = 0$, a lattice spanning quasi-equilibrium is formed and one expects the optimal bound to be entropic. In contrast, when $\epsilon$ is large the transition between lattice blocks is almost irreversible. In this case, a quasi-equilibrium is formed in each block separately, and one expects that the tightest bound will be achieved by taking entropy production terms for transitions within blocks and flux terms for transitions between blocks. Fig. 2(c) shows that this is indeed the case. For all parameters in this panel the kinetic bound performs poorly.

**Summary and discussion.** We have derived a TUR for first passage times. Our approach allows to consider models with completely irreversible transitions which are commonly used to study first passage problems. Crucially, we derive mixed bounds that combine kinetic and thermodynamic contributions from different transitions on the Markov network at hand. While the manuscript was being prepared, a different but related approach was used in [65] to derive a TUR for first passage times. Their results also apply for models of the type studied here. However, note that the TUR derived there is equivalent to the fully kinetic version of our bound, and is thus a special case. The results presented in Fig. 2, as well as the considerations below, suggest that the ability to also consider mixed bounds is important.

Our results show an interesting connection to another well known bound

$$CV^2 \geq \frac{1}{N},$$

where $N$ is again the number of kinetic states in the model (excluding the absorbing state). The bound (15) was proven by Aldous and Shepp (AS) [68], and is often used in the field of statistical kinetics [24–26]. Barato and Seifert [69] have shown that higher moments of first passage times also satisfy inequalities that depend on the number of states of the model.

We now discuss the relation between the TUR and the AS bound, with the help of the example depicted in Fig. 2. If all the transitions are irreversible, meaning $k_- = k_l = 0$, then one is forced to use the kinetic bound. In this case $\Sigma_{\text{uni}} = N = 5$ since the walker moves sequentially from the first site to the second, and continues moving right in this manner until it reaches the last site which is absorbing. We therefore recover the bound (15).

Using the kinetic bound when $k_-$ or $k_l$ are non-vanishing will give $\Sigma_{\text{uni}} > N$, and thus a bound which is looser than the AS bound. Yet, a mixed TUR bound can significantly improve on the AS result. Consider, for example, a scenario with $k_l = 0$ and $k_r,k_f \ll k_-,k_+$. These dynamics consist of fast local equilibration in two blocks of states: \{1, 2, 3\} and \{4, 5\}, and rare transitions between the blocks. Here, a mixed bound, which uses the entropy production from the blocks and the fluxes of the unidirectional transitions, is tightest. In such a configuration, one expects $\Sigma_{\text{uni}} = 2$ and $\Sigma_{\text{rev}} < 1$: The mixed TUR behaves as if it is an AS bound of a coarse-grained model with two effective kinetic states. This is consistent with the results depicted in Fig. 2(c).

Importantly, Markovian models are coarse-grained approximations of underlying microscopic dynamics. When several states of a model are almost always in local equilibrium with each other, thermodynamic consistency demands that we can coarse-grain them into one effective state, to obtain an even simpler model. The considerations above show how to get a TUR for coarse-grained models by appropriately partitioning transitions into two groups: uni- and bi-directional.

Finally, we note that several restrictions made on the model can be relaxed without many difficulties. The approach works for models with several physically distinct transitions between the same states. One simply needs to view these as separate transitions. It is also possi-
able to study models with irreversible transitions inside the network of transitions ([59, 70–72]). They do not need to lead to an absorbing state. Finally, one can also study models with several absorbing states. The derivation given in Ref. [59] generically shows how to handle such models.

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1 Redner, S., 2001. A guide to first-passage processes. Cambridge University Press, Cambridge, England.
2 Szabo, A., Schulten, K. and Schulten, Z., 1980. First passage time approach to diffusion controlled reactions. The Journal of chemical physics, 72(8), pp.4350-4357.
3 Szabo, A., Lamm, G. and Weiss, G.H., 1984. Localized partial traps in diffusion processes and random walks. Journal of statistical physics, 34(1), pp.225-238.
4 Nitzan, A., 2006. Chemical dynamics in condensed phases: relaxation, transfer and reactions in condensed molecular systems. Oxford university press.
5 Bénichou, O., Chevalier, C., Klafter, J., Meyer, B. and Voituriez, R., 2010. Geometry-controlled kinetics. Nature chemistry, 2(6), pp.472-477.
6 Scher, Y. and Reuveni, S., 2021. A Unified Approach to Gated Reactions on Networks. arXiv preprint arXiv:2101.05124.
7 Hopfield, J.J., 1974. Kinetic proofreading: a new mechanism for reducing errors in biosynthetic processes requiring high specificity. Proceedings of the National Academy of Sciences, 71(10), pp.4135-4139.
8 Ninio, J., 1987. Alternative to the steady-state method: derivation of reaction rates from first-passage times and pathway probabilities. Proceedings of the National Academy of Sciences, 84(3), pp.663-667.
9 Cao, J., 2011. Michaelis-Menten Equation and Detailed Balance in Enzymatic Networks. The Journal of Physical Chemistry B, 115(18), pp.5493-5498.
10 Murugan, A., Huse, D.A. and Leibler, S., 2012. Speed, dissipation, and error in kinetic proofreading. Proceedings of the National Academy of Sciences, 109(30), pp.12034-12039.
11 Reuveni, S., Urbakh, M. and Klafter, J., 2014. Role of substrate unbinding in Michaelis-Menten enzymatic reactions. Proceedings of the National Academy of Sciences, 111(12), pp.4391-4396.
12 Singh, D. and Chaudhury, S., 2017. Statistical properties of fluctuating enzymes with dynamic cooperativity using a first passage time distribution formalism. The Journal of chemical physics, 146(14), p.145103.
13 Robin, T., Reuveni, S. and Urbakh, M., 2018. Single-molecule theory of enzymatic inhibition. Nature communications, 9(1), pp.1-9.
14 Condamin, S., Bénichou, O., Tejedor, V., Voituriez, R. and Klafter, J., 2007. First-passage times in complex scale-invariant media. Nature, 450(7166), pp.77-80.
15 Eliazar, I., Koren, T. and Klafter, J., 2007. Searching circular DNA strands. Journal of Physics: Condensed Matter, 19(6), p.065140.
16 Bénichou, O., Loverdo, C., Moreau, M. and Voituriez, R., 2011. Intermittent search strategies. Reviews of Modern Physics, 83(1), p.81.
17 Chou, T. and D’Orsogna, M.R., 2014. First passage problems in biology. In First-passage phenomena and their applications (pp. 306-345).
18 Iyer-Biswas, S. and Zilman, A., First-Passage Processes in Cellular Biology, Advances in Chemical Physics, 160, Editors: S. A. Rice and A. R. Dinner, Wiley Online Library (2016).
19 Bray, A.J., Majumdar, S.N. and Schehr, G., 2013. Persistence and first-passage properties in nonequilibrium systems. Advances in Physics, 62(3), pp.225-361.
20 Metzler, R., Redner, S. and Oshanin, G. eds., 2014. First-passage phenomena and their applications (Vol. 35). World Scientific, Singapore.
21 Klafter, J. and Sokolov, I.M., 2011. First steps in random walks: from tools to applications. Oxford University Press, New York.
22 English, B.P., Min, W., Van Oijen, A.M., Lee, K.T., Luo, G., Sun, H., Cherayil, B.J., Kou, S.C. and Xie, X.S., 2006. Ever-fluctuating single enzyme molecules: Michaelis-Menten equation revisited. Nature chemical biology, 2(2), pp.87-94.
23 Kou, S.C., Cherayil, B.J., Min, W., English, B.P. and Xie, X.S., 2005. Single-molecule michaelis-menten equations.
24 Moffitt, J.R., Chemla, Y.R. and Bustamante, C., 2010. Methods in statistical kinetics. Methods in enzymology, 475, pp.221-257.
25 Moffitt, J.R., Chemla, Y.R. and Bustamante, C., 2010. Mechanistic constraints from the substrate concentration dependence of enzymatic fluctuations. Proceedings of the National Academy of Sciences, 107(36), pp.15739-15744.
26 Moffitt, J.R. and Bustamante, C., 2014. Extracting signal from noise: kinetic mechanisms from a Michaelis–Menten-like expression for enzymatic fluctuations. The FEBS journal, 281(2), pp.498-517.
27 Thorneycroft, A.L., Gladrow, J., Qing, Y., Rico-Pasto, M., Ritort, F., Bayley, H., Kolomeisky, A.B. and Keyser, U.F., 2020. Direct detection of molecular intermediates from first-passage times. Science advances, 6(18), p.eaaz4642.
28 Schnitzer, M.J. and Block, S.M., 1995, January. Statistical kinetics of processive enzymes. In Cold spring harbor symposia on quantitative biology (Vol. 60, pp. 793-802). Cold Spring Harbor Laboratory Press.
29 Shaeitz, J.W., Block, S.M. and Schnitzer, M.J., 2005. Statistical kinetics of macromolecular dynamics. Biophysical journal, 89(4), pp.2277-2285.
30 Kolomeisky, A.B. and Fisher, M.E., 2007. Molecular motors: a theorist’s perspective. Annu. Rev. Phys. Chem., 58, pp.675-695;
[31] Xu, W., Kong, J.S. and Chen, P., 2009. Single-molecule kinetic theory of heterogeneous and enzyme catalysis. The Journal of Physical Chemistry C, 113(6), pp.2393-2404.

[32] Yang, S., Cao, J., Silbey, R.J. and Sung, J., 2011. Quantitative interpretation of the randomness in single enzyme turnover times. Biophysical journal, 101(3), pp.519-524.

[33] Chaudhury, S., 2014. Poisson indicator and fano factor for probing dynamic disorder in single-molecule enzyme inhibition kinetics. The Journal of Physical Chemistry B, 118(35), pp.10405-10412.

[34] Reuveni, S., 2016. Optimal stochastic restart renders fluctuations in first passage times universal. Physical review letters, 116(17), p.170601.

[35] Pal, A. and Reuveni, S., 2017. First passage under restart. Physical review letters, 118(3), p.030603.

[36] Singh, D. and Chaudhury, S., 2018. Single-Molecule Kinetics of an Enzyme in the Presence of Multiple Substrates. ChemBioChem, 19(8), pp.842-850.

[37] Pal, A., Eliazar, I. and Reuveni, S., 2019. First passage under restart with branching. Physical review letters, 122(2), p.020602.

[38] Pal, A., Kusmierz, L. and Reuveni, S., 2020. Search with home returns provides advantage under high uncertainty. Physical Review Research, 2(4), p.043174.

[39] Sekimoto, K., 2010. Stochastic energetics (Vol. 799). Springer, Berlin.

[40] Seifert, U., 2012. Stochastic thermodynamics, fluctuation theorems and molecular machines. Reports on progress in physics, 75(12), p.126001.

[41] Jarzynski, C., 2011. Equalities and inequalities: Irreversibility and the second law of thermodynamics at the nanoscale. Annu. Rev. Condens. Matter Phys., 2(1), pp.329-351.

[42] Klages, R., Just, W. and Jarzynski, C., eds., 2013. Nonequilibrium statistical physics of small systems. Wiley-VCH Verlag GmbH & Company KGaA, Germany.

[43] Van den Broeck, C., and Esposito, M., 2015. Ensemble and trajectory thermodynamics: A brief introduction. Physica A, 418, pp.6-16.

[44] Ciliberto, S., 2017. Experiments in Stochastic Thermodynamics: Short History and Perspectives. Phys. Rev. X, 7, p.021051.

[45] Pezzato, C., Cheng, ., Stoddart, J. F., Astumian, R. D., 2017. Mastering the non-equilibrium assembly and operation of molecular machines. Chem. Soc. Rev., 46(18), pp.5491-5507.

[46] Barato, A.C. and Seifert, U., 2015. Thermodynamic uncertainty relation for biomolecular processes. Physical review letters, 114(15), p.158101.

[47] Gingrich, T.R., Horowitz, J.M., Perunov, N. and England, J.L., 2016. Dissipation bounds all steady-state current fluctuations. Physical review letters, 116(12), p.120601.

[48] Horowitz, J.M. and Gingrich, T.R., 2020. Thermodynamic uncertainty relations constrain non-equilibrium fluctuations. Nature Physics, 16(1), pp.15-20.

[49] Seifert, U., 2019. From stochastic thermodynamics to thermodynamic inference. Annual Review of Condensed Matter Physics, 10, pp.171-192.

[50] Horowitz, J.M. and Gingrich, T.R., 2017. Proof of the finite-time thermodynamic uncertainty relation for steady-state currents. Physical Review E, 96(2), p.020103.

[51] Pietzonka, P., Ritort, F. and Seifert, U., 2017. Finite-time generalization of the thermodynamic uncertainty relation. Physical Review E, 96(1), p.012101.

[52] Proesmans, K. and Van den Broeck, C., 2017. Discrete-time thermodynamic uncertainty relation. EPL (Europhysics Letters), 119(2), p.20001.

[53] Barato, A.C., Chetrite, R., Faggionato, A. and Gabrielli, D., 2018. Bounds on current fluctuations in periodically driven systems. New Journal of Physics, 20(10), p.103023.

[54] Dechant, A. and Sasa, S.I., 2018. Current fluctuations and transport efficiency for general Langevin systems. Journal of Statistical Mechanics: Theory and Experiment, 2018(6), p.063209.

[55] Hasegawa, Y. and Van Vu, T., 2019. Uncertainty relations in stochastic processes: An information inequality approach. Physical Review E, 99(6), p.062126.

[56] Ito, S. and Dechant, A., 2020. Stochastic time evolution, information geometry, and the Cramér-Rao bound. Physical Review X, 10(2), p.021056.

[57] Hasegawa, Y. and Van Vu, T., 2019. Fluctuation theorem uncertainty relation. Physical review letters, 123(11), p.110602.

[58] Falasco, G., Esposito, M. and Delvenne, J.C., 2020. Unifying thermodynamic uncertainty relations. New Journal of Physics, 22(5), p.053046.

[59] Pal, A., Reuveni, S. and Rahav, S., 2021. Thermodynamic uncertainty relation for systems with unidirectional transitions. Physical review Research 3, p.013273.

[60] Liu, K., Gong, Z. and Ueda, M., 2020. Thermodynamic uncertainty relation for arbitrary initial states. Physical Review Letters, 125(14), p.140602.

[61] Koyuk, T. and Seifert, U., 2020. Thermodynamic uncertainty relation for time-dependent driving. Physical Review Letters, 125(26), p.260604.

[62] Garrahan, J.P., 2017. Simple bounds on fluctuations and uncertainty relations for first-passage times of counting observables. Physical Review E, 95(3), p.032134.

[63] Gingrich, T.R. and Horowitz, J.M., 2017. Fundamental bounds on first passage time fluctuations for currents. Physical review letters, 119(17), p.170601.

[64] Falasco, G. and Esposito, M., 2020. Dissipation-time uncertainty relation. Physical Review Letters, 125(12), p.120604.

[65] Ken Hiura, and Shin-ichi Sasa, 2021. Kinetic uncertainty relation on first passage time for accumulated current arXiv preprint arXiv:2102.06398.

[66] Di Terlizzi, I. and Baiesi, M., 2018. Kinetic uncertainty relation. Journal of Physics A: Mathematical and Theoretical, 52(2), p.02LT03.

[67] Dechant, A. and Sasa, S.I., 2020. Fluctuation-response inequality out of equilibrium. Journal of Physics A: Mathematical and Theoretical, 53(2), p.02LT03.

[68] David, Aldous, and Shepp Larry. The least variable phase type distribution is Erlang. Stochastic Models 3, no. 3 (1987): 467-473.

[69] Barato, A.C. and Seifert, U., 2015. Skewness and kurtosis in statistical kinetics. Physical review letters, 115(18), p.188103.

[70] Rahav, S. and Harbola, U., 2014. An integral fluctuation theorem for systems with unidirectional transitions. Journal of Statistical Mechanics: Theory and Experiment, 2014(10), p.10044.

[71] Pal, A. and Rahav, S., 2017. Integral fluctuation theo-
rems for stochastic resetting systems. Physical Review E, 96(6), p.062135.

[72] Gupta, D., Plata, C.A. and Pal, A., 2020. Work fluctuations and Jarzynski equality in stochastic resetting. Physical review letters, 124(11), p.110608.