



# Time-information uncertainty relations in thermodynamics

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**Physical systems powering motion and creating structure in a fixed amount of time dissipate energy and produce entropy. Whether living, synthetic or engineered, systems performing these dynamic functions must balance dissipation and speed. Here, we show that rates of energy and entropy exchange are subject to a speed limit—a time-information uncertainty relation—imposed by the rates of change in the information content of the system. This uncertainty relation bounds the time that elapses before the change in a thermodynamic quantity has the same magnitude as its s.d. From this general bound, we establish a family of speed limits for heat, dissipated/chemical work and entropy depending on the experimental constraints on the system and its environment. In all of these inequalities, the timescale of transient dynamical fluctuations is universally bounded by the Fisher information. Moreover, they all have a mathematical form that mirrors the Mandelstam-Tamm version of the time-energy uncertainty relation in quantum mechanics. These bounds on the speed of arbitrary observables apply to transient systems away from thermodynamic equilibrium, independent of the physical constraints on the stochastic dynamics or their function.**

Many problems in science and engineering involve understanding how quickly a physical system transitions between distinguishable states and the energetic costs of advancing at a given speed. While theories such as thermodynamics and quantum mechanics put fundamental bounds on the dynamical evolution of physical systems, the form and function of the bounds differ. Clausius's version of the second law of thermodynamics<sup>1</sup>, for example, is an upper bound on the heat exchange in traversing equilibrium thermodynamics states—an inequality that limits the efficiency of heat engines without an explicit notion of time or fluctuations. By contrast, Mandelstam and Tamm's version of the time-energy uncertainty relation in quantum mechanics<sup>2,3</sup> is a limit on the speed at which quantum systems can evolve between two distinguishable quantum states. Given this important, and long-standing, contrast between these two pillars of physics, we explore thermodynamic bounds that are analogous to those in quantum mechanics, bounds that are independent of the system dynamics<sup>4–8</sup> and set limits on the speed of energy and entropy exchange.

Thermodynamic uncertainty relations<sup>9,10</sup> have been found where fluctuations in dynamical currents are bounded by the entropy production rate<sup>5,11–13</sup>. These relations apply to small systems and are part of stochastic thermodynamics<sup>14–18</sup>, a framework in which heat, work and entropy can be treated at the level of individual, fluctuating trajectories. Recent work has begun to suggest connections to the physics of information, information theory and information geometry<sup>6,8,19,20</sup>. In parallel to these discoveries, there have been advances in quantum-mechanical uncertainty relations or speed limits that constrain the speed at which dynamical variables evolve. They employ the mean<sup>3</sup>, variance<sup>2</sup> or higher-order moments of the energy<sup>21,22</sup>. These quantum speed limits, which also have information-theoretic forms, have recently been generalized to open quantum systems embedded in an environment<sup>23–26</sup>, paving the way for their application in the classical domain. The existence

of speed limits, regardless of the classical or quantum nature of the system, was first pointed out by Margolus<sup>22</sup>. Only recently have analogous bounds been established in classical systems and applied to Liouville dynamics in phase space<sup>27,28</sup> (also see related work<sup>29,30</sup>). While there has been rapid progress on thermodynamic uncertainty relations<sup>31</sup>, it remains to be seen whether there are speed limits in thermodynamics whose generality rivals those in quantum mechanics.

What governs the speed at which heat, work and entropy are exchanged between a system and its surroundings? Is there a universal quantity that bounds the speed at which thermodynamic observables evolve away from equilibrium? Motivated by these questions, we derive a family of limits to the speed with which a system can pass between distinguishable non-equilibrium states and the heat, work and entropy exchanged in the process.

## Equation of motion for thermodynamic observables

Consider a generic classical, physical system operating irreversibly, out of thermodynamic equilibrium. The stimulus for the time evolution of the physical system can be the removal of a constraint or the manipulation of an experimental control parameter  $\lambda$ , such as temperature or volume. As is common in stochastic thermodynamics<sup>15</sup>, we adopt a mesoscopic description and take the system to have a finite number of configurations  $x = 1, 2, \dots, N$  with initial probability  $p_x(t_0)$ . As currents in energy and matter cause the system to evolve, the probability distribution will generally differ from that of a Gibbsian ensemble. Our working assumption is that the dynamical evolution smoothly transforms the probability,  $p_x[\lambda(t)] = p_x(t) = p_x$ , of each state  $x$  at time  $t$  with a rate  $\dot{p}_x = dp_x/dt$ . All quantities here are time dependent unless explicitly stated otherwise.

During the non-equilibrium process, experimental measurements of an observable  $A$  for a classical system correspond to time-dependent statistical moments  $\langle A^n \rangle = \sum_x p_x a_x^n$  of the

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configuration observables  $a_x(t) = a_x$ . The Shannon entropy<sup>32</sup>, for example, is the expectation value of the surprisal  $I_x := -\ln p_x$ , which measures the information gained by observing the system in state  $x$ . With these minimal specifications, our first main result is that the ensemble average of any time-dependent observable  $A$  obeys an equation of motion,

$$\frac{d\langle A \rangle}{dt} = -\text{cov}(A, \dot{I}) + \left\langle \frac{dA}{dt} \right\rangle. \quad (1)$$

The covariance measures the linear correlation between  $A$  and the surprisal rate  $\dot{I}_x = dI_x/dt$ ,

$$-\dot{\mathcal{A}} := \text{cov}(\dot{I}, A) = \langle (A - \langle A \rangle)(\dot{I} - \langle \dot{I} \rangle) \rangle. \quad (2)$$

This evolution law makes no additional physical or modelling assumptions and holds for general processes away from thermodynamic equilibrium (see proof in Methods).

One form of the evolution equation is well known. For a system with a finite number of energy states,  $a_x \rightarrow e_x$ , it becomes the stochastic first law of thermodynamics,  $\dot{U} = d\langle e \rangle/dt = \dot{Q} + \dot{W}$  (ref. <sup>16</sup>). Energy exchanges between the system and external reservoirs are driven by mechanical forces,  $\dot{W}$ , and non-mechanical forces,  $\dot{Q} = \dot{Q} + \dot{W}_{\text{chem}} + \dots$ , including fluxes of heat  $\dot{Q}$  and chemical work  $\dot{W}_{\text{chem}}$  (ref. <sup>33</sup>). In what follows, we consider  $\dot{Q} = \dot{Q}$  and describe processes with non-zero chemical work in Methods. Comparing the first law with our result gives a statistical representation for the flux of work,  $\langle de/dt \rangle$ , and the flux of heat,  $\dot{Q} = \sum_x \dot{p}_x \delta e_x = -\text{cov}(\dot{I}, e)$ , where we have shifted the energy scale by the internal energy:  $\delta e_x := e_x - U$ . Thus, we find a new definition of energy exchanged between a system and its surroundings as heat: heat flux is a measure of the linear correlation between energy and information rates. While the covariance measures the linear relationship between random variables, it applies even when  $\dot{I}_x$  and  $e_x$  are nonlinearly related. Any quantity of the form of  $\mathcal{A} = \sum_x \dot{p}_x a_x$ , such as the entropy rate  $\dot{S}$ , can be expressed as this covariance.

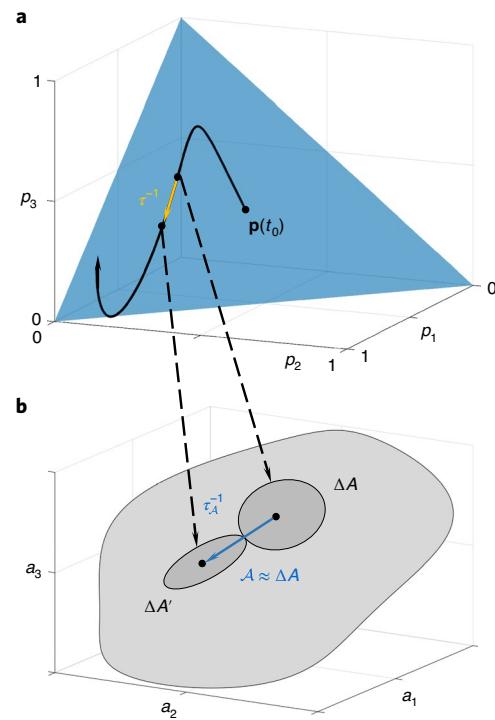
There is a striking similarity between the mathematical form of equation (1) and Ehrenfest's (Liouville's) theorem in quantum (classical) mechanics. Particularly important here is that the covariance fulfils the role of the mean commutator (Poisson bracket) of a quantum (classical) mechanical observable and the quantum (classical) Hamiltonian<sup>34</sup>. For this broad class of classical stochastic systems, the surprisal rate, not the Hamiltonian, is the observable with which all others are compared. If the probability distribution is canonical,  $P(x, t) = e^{-\beta H(x, t)}/Z(t)$ , however, they are proportional,  $\dot{I}(x, t) \propto -\beta H(x, t)$ . Given this analogy, we explore whether other relationships in quantum mechanics extend to classical, stochastic observables built on fluctuations and uncertainty.

### Observable fluctuations and evolution speed

As the non-equilibrium dynamics of the system unfold, observables will evolve in time (Fig. 1). From the equation of motion, a change in the state function  $\langle A \rangle$  is the result of two path functions. For the path function,  $\mathcal{A}$ , we define the instantaneous speed of evolution,

$$\frac{1}{\tau_{\mathcal{A}}} := \frac{|\dot{\mathcal{A}}|}{\Delta A} = \frac{|\text{cov}(\dot{I}, A)|}{\Delta A}, \quad (3)$$

in terms of the covariance in the equation of motion and the s.d.  $\Delta A$ . This timescale is the time required for  $A$  to evolve to a statistically distinguishable value. It has a form that is analogous to that for quantum-mechanical observables in the Mandelstam–Tamm time–energy uncertainty relation<sup>2,34</sup>. For any quantum-mechanical observable  $\hat{A}$  evolving under a Hamiltonian  $\hat{H}$  with s.d.  $\Delta \hat{H}$ , the Mandelstam–Tamm speed limit<sup>2</sup> bounds the timescale



**Fig. 1 | Speed limit from the statistical distinguishability of thermodynamic observables.** **a**, Away from thermodynamic equilibrium, stochastic dynamics will evolve a probability distribution over configurations, for example  $\mathbf{p}(t) = (p_1, p_2, p_3)$ , from  $t_0$  to  $t$ . The distribution evolves with a characteristic speed set by  $\sqrt{I_F} = \tau^{-1}$ , which measures the distinguishability of the distribution at two infinitesimally close times. **b**, Observables  $A$  of a system also evolve in time away from thermodynamic equilibrium. The distributions of  $A$  at two times are distinguishable in the sense used by Wootters<sup>37</sup> when the statistical distance between them is greater than their combined uncertainty:  $\text{dist}(A, A') \geq \Delta A + \Delta A'$  and  $A \neq A'$ , that is, when their s.d.s,  $\Delta A$  and  $\Delta A'$ , do not overlap. Here, the time  $\tau_A$  to reach a distinguishable state is when the path function  $|\mathcal{A}| = d\langle A \rangle/dt - \langle \dot{A} \rangle$  has the magnitude of  $\Delta A$ . The speed limit is  $\tau^{-1} \geq \tau_A^{-1}$ .

$\tau_{\mathcal{A}}$  over which the expectation value of the observable changes:  $\tau_{\mathcal{A}} \geq \tau_{\text{QM}} = \hbar/(2\Delta \hat{H})$ .

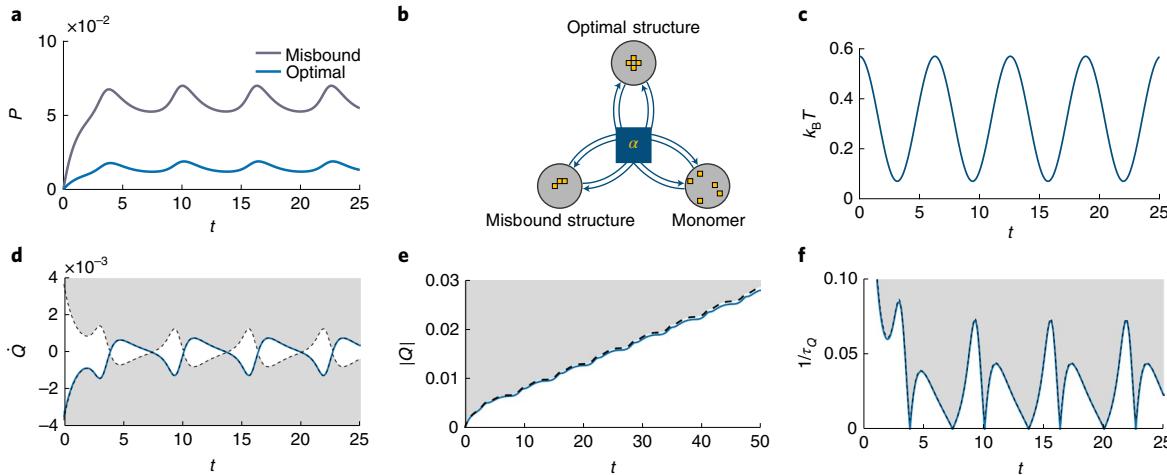
To understand the physical meaning of the timescale that we define,  $\tau_{\mathcal{A}}$ , suppose there is a constant flux  $\dot{\mathcal{A}}$ . Then, given two probability distributions  $\mathbf{p}(t)$  and  $\mathbf{p}(t_0)$ ,  $\tau_{\mathcal{A}}$  is the amount of time for the magnitude of the path function to have the value of one s.d.:

$$|\mathcal{A}| = \left| \int_{t_0}^{t_0 + \tau_{\mathcal{A}}} \dot{\mathcal{A}} dt \right| = |\dot{\mathcal{A}}| \tau_{\mathcal{A}} = \Delta A. \quad (4)$$

Despite the similarities so far, classical thermodynamic observables such as  $A$  do not yet have an analogous limit on the speed of their evolution. Because the general non-equilibrium distributions we consider may not have a direct connection to a Hamiltonian, it is natural to seek a characteristic time associated with the distinguishability of evolving probability distributions.

### Information fluctuations and intrinsic speed

The speed of each observable  $A$  measures its sensitivity to changes in the distribution over configurations (Fig. 1). To bound this speed for generic observables, one can consider the time required for the probability distribution to evolve to a distinguishable state<sup>35,36</sup>. There is evidence in both quantum<sup>23,37,38</sup> and classical<sup>39–41</sup> settings that the square root of the Fisher information<sup>42</sup>,  $\sqrt{I_F}$ , defines such



**Fig. 2 | Illustration of time-information uncertainty relation and speed limit for a model of driven assembly of monomeric units.** **a**, Probability of misassembled and optimally assembled states as a function of time for a three-state system of assembling particles in contact with a heat reservoir  $\alpha$  at temperature  $T$ . **b**, Model. The system has three possible states: dissociated monomeric units, misbound aggregates and an optimally bound configuration. An initial collection of monomers evolves, subject to a master equation dynamics and a periodic temperature protocol, and aggregates into a set of misbound structures and a single, optimally bound structure. **c**, Periodic temperature protocol over the same time span. **d**, At all times, equation (9),  $\pm \Delta \dot{I} \Delta \epsilon = \pm \Delta \epsilon / \tau$  (dashed line), upper and lower bounds the heat flux,  $\dot{Q}$  (blue line). **e**, Total absolute heat (blue) bounded by the integrated uncertainty bound equation (10) (dashed). **f**, The speed of heat exchange as a function of time (blue) is tightly bounded by the speed limit set by the Fisher information (dashed). In all plots, energy has the same units as  $k_B T$  units and time has the same units as those used in elements of the rate matrix.

a speed<sup>43</sup> for neighbouring, time-varying probability distributions that are a distance  $ds = \sqrt{I_F} dt$  apart. The Fisher information<sup>42</sup> is also a measure of fluctuations in the surprisal rate:

$$I_F := \sum_x^N p_x \left( \frac{d \ln p_x}{dt} \right)^2 = \Delta \dot{I}^2 =: \frac{1}{\tau^2}. \quad (5)$$

The surprisal rate only fluctuates for temporally varying distributions, that is, only in systems out of thermodynamic equilibrium. By the dimensional analysis above, fluctuations in the information content,  $1/\Delta \dot{I} = 1/\sqrt{I_F}$ , set an intrinsic timescale for the evolution of the probability distribution in systems out of equilibrium,  $\tau := 1/\sqrt{I_F}$  (refs. <sup>40,41,44</sup>). However, does this timescale provide a general bound on the speed at which non-equilibrium observables evolve?

### Time-information uncertainty relation and speed limit

With the results above, we can place bounds on the uncertainty in thermodynamic observables, regardless of the dynamical variable or the stochastic dynamical law governing the probability distribution over configurations. The fluctuations in  $A$  and  $\dot{I}$  upper bound their covariance through the inequality

$$|\dot{A}| = |\text{cov}(\dot{I}, A)| \leq \Delta \dot{I} \Delta A. \quad (6)$$

This time-information uncertainty relation for  $A$  depends on the fluctuations in the surprisal rate,  $\Delta \dot{I} = \sqrt{I_F}$ , and holds for a variety of thermodynamic fluxes: heat  $\dot{Q}$ , dissipated work  $\dot{W}_{\text{diss}}$ , chemical work  $\dot{W}_{\text{chem}}$  and entropy  $\dot{S}$ .

As an immediate consequence of this uncertainty relation, fluctuations in the surprisal rate  $\Delta \dot{I} = 1/\tau$  are an upper bound on the instantaneous speed of any dynamical variable that is a covariance with the surprisal rate:

$$\Delta \dot{I} \geq 1/\tau_A. \quad (7)$$

The Fisher information is a property of the distribution over configurations that evolves with stochastic dynamics. Moreover, this classical uncertainty relation,  $\tau_A \Delta \dot{I} \geq 1$ , sets the intrinsic timescale that bounds the timescale of all other dynamical quantities: a system out of thermodynamic equilibrium with a spread  $\Delta \dot{I} = \sqrt{I_F}$  in surprisal rate takes a time of at least  $\tau_A \geq 1/\sqrt{I_F}$  for the path function  $|\dot{A}|$  to change by  $\Delta A$ . A small (large) spread in surprisal rates sets a lower (higher) speed limit on  $A$  through  $\dot{A}$ .

Again, there are parallels with quantum mechanics. The Mandelstam–Tamm bound  $\tau_A \geq \hbar/(2\Delta \hat{H})$  can also be expressed in terms of the quantum Fisher information  $\hat{I}_F$ . For pure states evolving under a unitary dynamics, the quantum Fisher Information is  $\hat{I}_F = 4\Delta \hat{H}^2/\hbar^2$  (refs. <sup>38,45</sup>), and the quantum version of the bound,  $\tau_A \geq 1/\sqrt{\hat{I}_F}$ , is formally identical to this classical speed limit.

While it is analogous to the quantum speed limit, the time-information speed limit applies immediately to the fluxes of thermodynamic quantities. The time-information speed limit assumes a differentiable distribution but it makes no model assumptions about the stochastic dynamics, the proximity to equilibrium, the size of the system or the protocol driving the system out of equilibrium. As we show in Methods, a sufficient condition to saturate the bound, and achieve the speed limit, is a linear relationship between  $\dot{I}$  and  $A$ . The nature of the non-equilibrium drive, physical constraints on the system, and exchanges of energy and entropy between the system and its environment control the speed limit.

At one extreme, thermodynamic fluxes converge to constant values, sustained by an external drive and a constant current through the system. When the system is at equilibrium or in non-equilibrium steady states with a finite  $\Delta A$ , the uncertainty in the surprisal rate vanishes,  $\Delta \dot{I} = 0$ . No matter what  $A$  is being considered,  $|\dot{A}| = 0$  and the timescale  $\tau_A$  diverges. At steady state, the covariance  $\dot{A} = -\text{cov}(\dot{I}, A)$  vanishes. By analogy, stationary states in classical mechanics correspond to a vanishing Poisson bracket and a stationary phase space density.

At the other extreme, the system is driven strongly, transiently and perhaps with large fluctuations that prevent macroscopic

observables from establishing steady values. If observables exhibit a rapid variation with time, then the underlying distribution over configurations must have large fluctuations in the surprisal rates and a large Fisher information. When the system is driven quickly through non-equilibrium states such that  $|\dot{\mathcal{A}}| \rightarrow \infty$ , the timescale  $\tau_{\mathcal{A}} \rightarrow 0$ . Accomplishing such an extreme change in the mean requires a corresponding change in the distribution and  $\Delta\dot{I} \rightarrow \infty$ .

Between these limits, integrating the uncertainty relation yields connections between measurable thermodynamic quantities. A given non-equilibrium process, regardless of the driving protocol or specific dynamics, evolves the probability distribution over the system configurations. The system traverses a probability manifold (Fig. 1a), which is not a manifold of equilibrium states because the distribution at each point on the manifold need not correspond to a Gibbsian distribution. Over a time interval  $t_f - t_0$  with the arbitrary initial and final probability distributions  $\mathbf{p}(t_0)$  and  $\mathbf{p}(t_f)$ , it follows from the time-information uncertainty relation that

$$|\mathcal{A}| = \left| \int_{t_0}^{t_f} \dot{\mathcal{A}} dt \right| \leq \int_{t_0}^{t_f} \Delta\dot{I} \Delta A dt = \int_{\mathbf{p}(t_0)}^{\mathbf{p}(t_f)} \Delta A ds. \quad (8)$$

The integrated path function  $|\mathcal{A}|$  is bounded by the cumulative fluctuations in  $A$  over the path taken by the system across the probability manifold.

### Cramér–Rao inequality in estimation theory

The time-information uncertainty relation is a bound on the speed at which time-dependent macroscopic quantities  $A$  can evolve between distinguishable states. A related, but distinct, question from estimation theory is how to efficiently estimate a parameter  $\theta$  of a distribution. There, the Fisher information provides a lower bound on the efficiency of all estimators,  $\dot{\theta}$ , through the Cramér–Rao inequality  $\partial_{\theta} \langle \dot{\theta} \rangle_{\theta} \leq \Delta\dot{\theta} \sqrt{T_F}$ . Like other uncertainty relations<sup>8,19</sup>, there are connections between equation (6) and the Cramér–Rao bound.

There is a direct connection when one considers a thermodynamic observable,  $a_x(t)$ , as an estimator for time,  $\theta = t$  (ref. <sup>46</sup>). Then, if the estimator  $a_x(t) = a_x$  is time independent, the Cramér–Rao inequality follows from the uncertainty relation in equation (6). Physically, this case corresponds to the second path function in equation (1),  $\langle dA/dt \rangle = 0$ , being zero; if the observable of interest is the energy, for example, then the Cramér–Rao bound applies to processes in which there is no work done on or by the system. Mathematically, this case requires the estimator to be sufficient. Sufficient estimators are usually assumed in deriving the Cramér–Rao bound<sup>47,48</sup> due to their superior point estimates of an unknown parameter. The uncertainty relation in equation (6) does not have these requirements and holds regardless of whether the protocol, observables, path functions or probability distribution are time dependent.

The uncertainty relation and the stochastic speed limit have particular physical meaning within thermodynamics. We establish a family of time-information uncertainty relations including incarnations for the flux of chemical and dissipated work (Methods). Thermodynamics has specific representations depending upon the experimental conditions, which set the natural variables and appropriate thermodynamic potential<sup>1</sup>. Here, we focus on representations for energy and entropy.

### Thermodynamic observables

When there are only energy exchanges within the system, or between the system and its surroundings, the uncertainty relation for the rate of heat exchange,

$$|\dot{Q}| = |\text{cov}(\dot{I}, \epsilon)| \leq \Delta\dot{I} \Delta\epsilon, \quad (9)$$

is upper bounded by the s.d.s in the surprisal rate  $\Delta\dot{I}$  and energy  $\Delta\epsilon$ . At stationary states, where  $\dot{Q} = 0$  and  $\dot{p}_x = 0 \forall x$ , the heat flux into the system balances the heat flux out and the bound is trivially saturated. Away from stationary states, the product of the information rate and energy fluctuations limits the rate at which energy can be absorbed or dissipated as heat. The speed limit,  $\tau^{-1} \geq |\dot{Q}|/\Delta\epsilon$ , determines the maximum relative heat flux. Moreover, integrating the heat exchanged along a particular path on the probability manifold, the total heat  $Q$  exchanged is bounded by the cumulative energy fluctuations:

$$|Q| \leq \int_{\mathbf{p}(t_0)}^{\mathbf{p}(t_f)} \Delta\epsilon ds, \quad (10)$$

with no restrictions on the initial, final or intervening distributions visited during the non-equilibrium process. When heat and work are non-zero, the first law can be used to recast these results in terms of the rates of internal energy and work. For example, equation (9) is  $|\dot{U} - \dot{\mathcal{W}}| \leq \Delta\dot{I} \Delta\epsilon$ , which simplifies if internal energy is conserved,  $|\dot{\mathcal{W}}| \leq \Delta\dot{I} \Delta\epsilon$ , or if no work is done,  $|\dot{U}| \leq \Delta\dot{I} \Delta\epsilon$ .

There is a complementary uncertainty relation for entropy exchange. As the ensemble average of the surprisal, the Shannon entropy  $S/k_B = -\sum_x p_x \ln p_x$  also satisfies the equation of motion, equation (1). The entropy is a case where only the covariance term survives in the equation of motion (as we show in Methods) and the rate of change of the entropy measures the linear correlation between the surprisal and its speed. Thus, the entropy rate,

$$|\dot{S}|/k_B = |\text{cov}(\dot{I}, I)| \leq \Delta\dot{I} \Delta I, \quad (11)$$

is bounded by the spread in information-theoretic quantities, the surprisal and its rate of change. The timescale  $\tau_S = k_B \Delta I / |\dot{S}| \leq 1 / \Delta\dot{I}$  measures the time needed for the Shannon entropy to change by one s.d. in the surprisal fluctuations.

A common approach in non-equilibrium thermodynamics<sup>49</sup> is to divide the rate of entropy change for the system into the rate of entropy production internal to the system  $\dot{S}_i$  (the irreversible entropy production rate) and the rate of entropy exchanged with the surroundings  $\dot{S}_e$  (the entropy flow rate):  $\dot{S} = \dot{S}_i + \dot{S}_e$ . In the special case where  $\dot{S}_i = 0$  (for example a reversible process), it follows that  $|\dot{S}_e|/k_B \leq \Delta\dot{I} \Delta I$ . Likewise, when  $\dot{S}_e = 0$  (for example symmetric Markovian dynamics), the entropy production rate is bounded by fluctuations in the surprisal and surprisal rate  $\dot{S}_i/k_B \leq \Delta\dot{I} \Delta I$ .

To illustrate our results, we analytically solved a two-state model (Supplementary Section I). We also numerically solved a model for non-equilibrium self-assembly under periodic driving of the temperature, thermal relaxation and thermal annealing (Supplementary Sections II and III). The time-information uncertainty relation and associated speed limit for flows of heat (Fig. 2) and entropy hold regardless of the dynamics or driving protocol.

### Conclusions

According to thermodynamics, every natural process faces the physical principle that structure formation or useful work production, at a particular speed, comes at a cost: entropy production, energy dissipated as heat, and wasted free energy. Here, we have shown that these thermodynamic costs are restricted by fluctuations and satisfy a time-information uncertainty relation. The mathematical form of this relation is similar to the Mandelstam–Tamm version of the time-energy uncertainty relation, an important milestone in quantum mechanics. Because our formalism similarly requires few details about the model system or the experimental conditions, we expect it to be applicable to a broad range of physical and (bio) chemical systems. With no assumption about the underlying model dynamics or external driving protocol, it can also be applied to any non-equilibrium process with a differentiable probability

distribution. The uncertainty relations we derived for the flux of heat, entropy and work (both dissipated and resulting from material transport or chemical reactions) demonstrate that the timescales of their dynamical fluctuations away from equilibrium are all bounded by the fluctuations in information rates. Therefore, while away from equilibrium, natural processes must trade speed for thermodynamic costs.

## Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41567-020-0981-y>.

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## Methods

**Equation of motion.** The surprisal rate is defined as  $\dot{I}_x = -d \ln p_x / dt$ . Its mean is zero,

$$-\langle \dot{I} \rangle = \sum_x^N p_x \frac{d \ln p_x}{dt} = \sum_x^N \frac{dp_x}{dt} = \frac{d}{dt} \sum_x^N p_x = 0 \quad (12)$$

as a consequence of the conservation of probability,  $\sum_x^N p_x = 1$ . Using these two facts, the equation of motion for the expectation value of an observable is:

$$\begin{aligned} \frac{d}{dt} \langle A \rangle &= -\langle \dot{I} A \rangle + \langle \frac{dA}{dt} \rangle \\ &= -\langle \dot{I} A \rangle + \langle \dot{I} \rangle \langle A \rangle + \langle \frac{dA}{dt} \rangle \\ &= -\text{cov}(\dot{I}, A) + \langle \frac{dA}{dt} \rangle. \end{aligned} \quad (13)$$

The final expression is equation (1) in the main text. A covariance of zero indicates that two variables are uncorrelated. It does not necessarily mean that they are statistically independent, since random variables that are nonlinearly related can also be uncorrelated.

**Entropy rate as a covariance.** The Shannon entropy is the ensemble average

$$S/k_B = -\sum_x^N p_x \ln p_x = \langle -\ln p \rangle = \langle I \rangle \quad (14)$$

of the surprisal  $I_x = -\ln p_x$ . Using  $\langle \dot{I} \rangle = 0$ , its rate of change,

$$\begin{aligned} \dot{S}_B &= -\sum_x^N \dot{p}_x \ln p_x - \sum_x^N p_x \frac{d \ln p_x}{dt} \\ &= -\langle \dot{I} I \rangle + \langle \dot{I} \rangle \langle I \rangle \\ &= -\text{cov}(\dot{I}, I), \end{aligned} \quad (15)$$

can be expressed as the (negative) covariance of the surprisal and the surprisal rate.

**Geometric interpretation of the Fisher information.** The Fisher information parameterized by time is a measure of distance  $ds$  between neighbouring distributions,

$$ds^2 = \sum_{ij} \frac{d^2 I}{dt^2} g_{ij} \frac{d\lambda^j}{dt} dt^2 = I_F dt^2, \quad (16)$$

where the Fisher metric is

$$g_{ij} = \left\langle \frac{\partial \ln p_x}{\partial \lambda_i} \frac{\partial \ln p_x}{\partial \lambda_j} \right\rangle. \quad (17)$$

This statistical distance can be interpreted as a measure of the distinguishability between  $p_x(t)$  and  $p_x(t+dt)$  (refs. <sup>37,43</sup>). Looking at the physical dimensions,  $\sqrt{I_F}$  is a 'speed' relating the dimensionless  $ds$  and infinitesimal increment of time  $dt$ .

**Saturation of the uncertainty relation and speed limit.** The uncertainty in equation (6),  $|\mathcal{A}| \leq \Delta \dot{I} \Delta A$ , is independent of the form of the distribution. A sufficient condition to saturate the bound, and achieve the speed limit, is a linear relationship between  $\dot{I}$  and  $A$ . A linear relationship between these variables implies that the probability distribution is of the form

$$p_x(t) = C \exp \left[ - \int_{t_0}^t c_a \delta a_x dt' \right] \quad (18)$$

with  $c_a = \Delta \dot{I} / \Delta A = -\dot{A} / \Delta A^2$ . The normalization factor  $C$  enforces the initial condition  $p_x(t_0)$  and the conservation of probability  $\sum_x^N p_x(t) = 1$ . Exponential probability distributions that are linear in the argument  $a_x$  saturate the uncertainty relation, even when they are time dependent.

To prove these statements, we derive the covariance inequality for  $\dot{I}$  and  $A$  and show that this bound saturates when these random variables are linearly related. Consider the standardized variables

$$\dot{I}'_x = \frac{\dot{I}_x}{\Delta \dot{I}} \quad a'_x = \frac{a_x - \langle A \rangle}{\Delta A}$$

The expectation and s.d. of both standardized variables is  $\langle \dot{I}' \rangle = \langle A' \rangle = 0$  and  $\Delta \dot{I}' = \Delta A' = 1$ . Defining the correlation as  $\rho(X, Y) \equiv \text{cov}(X, Y) / \Delta X \Delta Y$  and using the identity  $\Delta(X - Y)^2 = \Delta(X)^2 + \Delta(Y)^2 - 2 \text{cov}(X, Y)$ , we have

$$\begin{aligned} \Delta(\dot{I}' - A')^2 &= \Delta \dot{I}' + \Delta A' - 2 \text{cov}(\dot{I}', A') \\ &= 2[1 - \rho(\dot{I}', A')] \\ &= 2[1 - \rho(\dot{I}, A)]. \end{aligned} \quad (19)$$

The last line is a result of the fact that standardizing random variables does not change the correlation  $\rho(X', Y') = \rho(X, Y)$ . Thus, the condition  $\rho(\dot{I}', A') = 1$  is equivalent to  $\Delta(\dot{I}' - A')^2 = 0$ . A zero variance means  $\dot{I}' = a'$  with unit

probability. Taking the expectation of  $\dot{I}'_x - a'_x$ , we see that  $\langle \dot{I}' - A' \rangle = 0$ . As a result,  $\dot{I}' = a' \forall x$ , or

$$\dot{I}_x = \frac{\Delta \dot{I}}{\Delta A} a_x - \frac{\Delta \dot{I}}{\Delta A} \langle A \rangle \equiv c_a \delta a_x. \quad (20)$$

We can now find the distribution that saturates the time-information uncertainty bound for  $A$ . From equation (20) we have the equation of motion

$$\dot{p}_x(t) = -c_a \delta a_x p_x(t) \quad (21)$$

with the solution in equation (18). In the integrand,  $c_a = \Delta \dot{I} / \Delta A$ . By construction this distribution saturates the bound, so that  $\mathcal{A} = -\Delta \dot{I} \Delta A$  and  $c_a = -\mathcal{A} / \Delta A^2$ .

Using the definitions of  $\tau_A$  and  $\tau$ , saturating the bounds implies that the timescales of the system and observable are equal, that is,  $\tau = \tau_A$  and  $|\dot{A}| = \Delta \dot{I} \Delta A$ .

**Bounds for a time-dependent Boltzmann distribution.** Exponential distributions characteristic of Gibbsian ensembles are a subset of the distributions that saturate the uncertainty relation. Consider a system in thermal contact with a reservoir at a temperature  $\beta^{-1}$  that is varied over time and evolves the distribution over fixed energy states. If the Boltzmann form of the distribution is preserved during this process, the probability of a configuration  $x$  with fixed energy  $\epsilon_x$  is  $p_x(t) = e^{-\beta(t) \epsilon_x} / Z(t)$ . In this case, the bound is saturated in both energy and entropy representations. The pertinent quantities are:

$$\begin{aligned} \dot{p}_x &= -\left(\dot{\beta} \epsilon_x + \frac{\dot{Z}}{Z}\right) p_x & I_x &= \beta \epsilon_x + \ln Z \\ \dot{I}_x &= \dot{\beta} \epsilon_x + \frac{\dot{Z}}{Z} & S &= \beta U + \ln Z, \\ \dot{Z} &= -\dot{\beta} \sum_x^N \epsilon_x e^{-\beta \epsilon_x} & \frac{\dot{Z}}{Z} &= -\dot{\beta} U \end{aligned} \quad (22)$$

From these relations, the heat flux is:

$$\dot{Q} = \sum_x^N \dot{p}_x \delta \epsilon_x = -\dot{\beta} \Delta \epsilon^2. \quad (23)$$

As stated in the main text, the negative covariance of  $\dot{I}$  and  $\epsilon$ ,

$$-\text{cov}(\dot{I}, \epsilon) = -\sum_x^N p_x \dot{I}_x \delta \epsilon_x = -\dot{\beta} \Delta \epsilon^2, \quad (24)$$

is equal to  $\dot{Q}$ . We can arrive at the same result using equation (20). Starting with  $c_a = \Delta \dot{I} / \Delta A = \sqrt{I_F} / \Delta A$ , the Fisher information is

$$I_F = \sum_x^N \frac{\dot{p}_x^2}{p_x} = \dot{\beta}^2 \Delta \epsilon^2, \quad (25)$$

which makes the surprisal rate  $\dot{I}_x = \dot{\beta} \epsilon_x - \dot{Z} / Z$ . The covariance with  $\epsilon$  follows as above to give  $\dot{Q}$ .

Next, the entropy rate for this exponential distribution

$$\dot{S}/k_B = \sum_x^N \dot{p}_x \delta I_x = \beta \dot{Q}, \quad (26)$$

recovers the equilibrium relationship between entropy and heat. Using equation (23) we also find that the change in entropy can be written as  $\dot{S} = -\beta \dot{\beta} \Delta \epsilon^2$ . The covariance between  $\dot{I}$  and  $I$ ,

$$\text{cov}(\dot{I}, I) = \sum_x^N p_x \dot{I}_x (I_x - S) = \beta \dot{\beta} \Delta \epsilon^2 \quad (27)$$

confirms that  $\dot{S} = -\text{cov}(\dot{I}, I)$ . Finally, looking at the right-hand side of the entropic uncertainty relation, we have the fluctuations in the surprisal and its rate:

$$\Delta I^2 = \sum_x^N p_x (I_x - S)^2 = \beta^2 \Delta \epsilon^2 \quad (28)$$

$$\Delta \dot{I}^2 = \sum_x^N p_x \dot{I}_x^2 = \dot{\beta}^2 \Delta \epsilon^2. \quad (29)$$

The uncertainty relations in the energy and entropy representations,

$$\begin{aligned} \dot{Q} &= -\Delta \dot{I} \Delta \epsilon = \dot{\beta} \Delta \epsilon^2 \\ \dot{S}/k_B &= -\Delta \dot{I} \Delta I = \beta \dot{\beta} \Delta \epsilon^2 \end{aligned} \quad (30)$$

together then give  $\dot{S}/k_B = \beta \dot{Q}$ , the well known definition of the thermodynamic entropy and the lower bound of the Clausius inequality for reversible processes<sup>1</sup>.

When the bound saturates, the evolution of the system is operating at the speed limit. The evolution time for the observable is equal to the timescale set by the Fisher information, that is,  $\tau = \tau_A$ . For the time-dependent Boltzmann distribution considered here,

$$\tau = \frac{1}{\Delta \dot{I}} = \frac{1}{|\dot{\beta}| \Delta \epsilon} = \frac{\Delta \epsilon}{|\dot{Q}|} = \tau_Q. \quad (31)$$

The time for the heat to evolve by one energy fluctuation is exactly the time it takes the distribution to evolve to a distinguishable state. These timescales are also equal to the speed of the entropy  $\tau_S = k_B \Delta I / |\dot{S}| = \tau = \tau_Q$ . A quasistatic process is then one whose thermodynamic timescales are equivalent to the statistical timescale  $\tau$ . For this special driving protocol, the rate of change in the inverse temperature is precisely the heat flow relative to the energy fluctuations:  $|\dot{\beta}| = |\dot{Q}| / \Delta \epsilon^2$ .

**Uncertainty relations for work.** *Chemical work.* The formalism also applies to open systems in which non-mechanical forces drive the flux of matter. Consider an open, thermally conducting system with a single chemically independent constituent that is exchanged with the environment. The non-mechanical energy flux will have contributions that account for the heat and matter exchange in the chemical work with an external reservoir,

$$\dot{Q} = \dot{Q} + \dot{W}_{\text{chem}} = \sum_x \dot{p}_x \epsilon_x. \quad (32)$$

The stochastic chemical work,  $\dot{W}_{\text{chem}} = \sum_{x,k} \mu^k n_x \dot{p}_x$ , is mediated by the chemical potential of the  $k$ th reservoir,  $\mu^k$ , and the number of molecules in state  $x$ ,  $n_x$  (ref. <sup>16</sup>). Because the chemical work has the form of  $\dot{A}$ , it has a covariance representation  $\dot{W}_{\text{chem}} = -\text{cov}(\dot{I}, g)$ , where  $g_x^k = \mu^k n_x$  is the contribution to the Gibbs free energy of state  $x$ . The time-information uncertainty relation follows immediately,  $|\dot{W}_{\text{chem}}| = |\text{cov}(\dot{I}, g)| \leq \Delta \dot{I} \Delta g$ . The heat flux for such an open system,

$$\dot{Q} = -\text{cov}(\dot{I}, \epsilon - g) = \text{cov}(\dot{I}, g) - \text{cov}(\dot{I}, \epsilon), \quad (33)$$

leads to the uncertainty relation:

$$|\dot{Q}| = |\text{cov}(\dot{I}, \epsilon - g)| \leq \Delta \dot{I} \Delta (\epsilon - g). \quad (34)$$

Fluctuations in energy and matter are not necessarily independent and the timescale for the heat flux is more complicated than in closed systems,  $\tau_Q^{-1} = |\dot{Q}| / \Delta(\epsilon - g)$ .

If the energy fluctuations are fixed and of order  $k_B T$ , then the speed  $\tau_Q^{-1} = |\dot{Q}| / k_B T$  is bounded by the fluctuations in surprisal rate,  $\beta |\dot{Q}| \leq \Delta \dot{I}$ . In other words, fluctuations in the surprisal rate constrain non-equilibrium heat flow.

**Dissipated work.** The tendency of physical systems to increase entropy can be harnessed to do useful work. However, unless the process is thermodynamically reversible, some energy will be dissipated. For a system in contact with a heat bath at fixed  $T = 1/k_B \beta$ , the non-equilibrium free energy is  $F = U - \beta^{-1} S$  (ref. <sup>15</sup>). The rate of dissipated work or dissipated power,  $\dot{W}_{\text{diss}} = \dot{W} - \dot{F}$ , also satisfies a time-information uncertainty relation.

Using our results for the fluxes of heat and entropy, the dissipated power,

$$\beta \dot{W}_{\text{diss}} = \beta \text{cov}(\dot{I}, \epsilon) - \text{cov}(\dot{I}, I), \quad (35)$$

is the difference in the linear correlation of the information and the energy with  $\dot{I}$ . The time-information uncertainty relation is found using the triangle inequality and the Clausius inequality  $|\dot{S}| / k_B \geq \beta |\dot{Q}|$ :

$$\beta |\dot{W}_{\text{diss}}| \leq |\dot{S}| / k_B + \beta |\dot{Q}| \leq 2 \Delta \dot{I} \Delta I. \quad (36)$$

Again, the rate of change in the information content of the distribution is the reference for a thermodynamic observable.

**Model systems and dynamics.** The self-assembly model we chose<sup>50</sup> allows us to analyse the energy exchanged as heat during an assembly process under arbitrary protocols. The system can be found in three possible states  $x$ : dissociated monomeric units, misbound aggregates and an optimally bound configuration, which we denote by  $x_1$ ,  $x_2$  and  $x_3$ , respectively. Initially the system consists purely of monomers. As the system evolves, the temperature is changed according to a given

protocol and monomers transition into the assembled states. Despite the simplicity of the model, the dynamics captures the competition between kinetic trapping and binding strength, a phenomenon also exhibited in more complicated models, such as those for chaperonin proteins<sup>50</sup>.

While not necessary for the theory, we take the dynamics to be governed by the master equation,  $\dot{p}(t) = \Omega(t)p(t)$ . The rate matrix  $\Omega$  has non-negative off-diagonal elements and satisfies  $\Omega_{xx}(t) = -\sum_{x \neq y} \Omega_{xy}(t)$ , which guarantees conservation of probability. Its elements,

$$\Omega = \begin{pmatrix} -c(M+1) & \alpha & \alpha^2 \\ cM & -\alpha & 0 \\ c & 0 & -\alpha^2 \end{pmatrix}, \quad (37)$$

include a concentration-like variable  $c = 0.02$ , the number of possible misbound states  $M = 5$  and  $\alpha = \exp(-\epsilon_b/2T)$ , a function of the binding strength  $\epsilon_b = 0.1$  and  $T$  with  $k_B = 1$ . Consider a periodic variation of the temperature over time (Fig. 2a), with  $T(t) = \gamma_1 \cos(t) + \gamma_2$ , and  $\gamma_1 = 0.25$  and  $\gamma_2 = 0.32$  to keep the temperature in the range used in ref. <sup>50</sup>. As a result of this driving protocol, the probabilities of occupying the misbound state and optimally bound states also oscillate in time (Fig. 2b). The probability of observing the monomer state also oscillates after a brief decay for the initial value of one.

## Data availability

The data sets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

## Code availability

The codes generated and used during the current study are available from the corresponding author on reasonable request.

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## Author contributions

S.B.N., L.P.G.P., A.d.C. and J.R.G. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

## Competing interests

The authors declare no competing interests.

## Additional information

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