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Thermodynamic uncertainty relations constrain non-equilibrium fluctuations

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In equilibrium thermodynamics, there exists a well-established connection between dynamical fluctuations of a physical system and the dissipation of its energy into an environment. However, few similarly quantitative tools are available for the description of physical systems out of equilibrium. Here, we offer our perspective on the recent development of a new class of inequalities known as thermodynamic uncertainty relations, which have revealed that dissipation constrains current fluctuations in steady states arbitrarily far from equilibrium. We discuss the stochastic thermodynamic origin of these inequalities, and highlight recent efforts to expand their applicability, which have focused on connections between current fluctuations and the fluctuation theorems.

Our understanding of the properties of macroscopic equilibrium systems is built on a collection of general principles. The Boltzmann distribution allows one to predict thermodynamic properties of a system — such as its temperature or pressure — without having to solve any dynamical equations. The second law of thermodynamics places constraints on what thermodynamic processes are physically realizable: only those that increase entropy. From it, we gain insight into the design principles of devices, such as the Carnot bound on the efficiency of any thermodynamic heat engine.

By contrast, small systems — be it a single Brownian particle, a molecular motor or a handful of chemical reactions — are strongly affected by their surroundings, causing them to fluctuate violently, often quite far from equilibrium. While there is no simple formula like the Boltzmann distribution for non-equilibrium systems, elucidating generic thermodynamic constraints on non-equilibrium dynamics, like the second law, can allow us to unravel some of the basic principles of non-equilibrium behaviour.

In this regard, there is now a growing catalogue of general quantitative predictions about non-equilibrium fluctuations. While fluctuations may seem like incoherent noise, we are now learning that thermodynamics imbues them with predictable structure. Perhaps the most prominent examples are the fluctuation theorems, which are symmetries of the fluctuations in thermodynamic observables, like the amount of heat transferred between a system and reservoir[1–3]. They not only reveal a fundamental property of thermodynamic fluctuations but also have led to the development of novel experimental and computational techniques that utilize driven non-equilibrium processes to measure equilibrium properties, such as free energies.

Here, we discuss a recently discovered collection of inequalities that offer related constraints on the fluctuations of currents in non-equilibrium steady states. Christened the thermodynamic uncertainty relations (TURs), these inequalities give limits on the precision of non-equilibrium currents in terms of the dissipation, or entropy production, of the non-equilibrium system[4].

In the time since the TUR was first proved[5], a flurry of follow-up results have further illuminated the origins of the inequality and the potential applicability to non-equilibrium thermodynamics. We offer our perspective on the state of the art, addressing how various TUR results fit together, how they might be applied and how they could be extended.

Stochastic thermodynamics

Imagine a non-equilibrium system coupled to an environment with which it can exchange particles, heat, charge and so on, like the one in Fig. 1a. Configurational changes of the system are then intrinsically linked to these exchanges. For example, if the transition requires the system's energy to increase, that energy must be supplied by the environment as heat. The theoretical framework of stochastic thermodynamics codifies this connection between the dynamical description of the system and the thermodynamics of the environment[1–3]. It allows one to consistently investigate fluctuations in the energetics and thermodynamics of non-equilibrium systems.

The first step of such an analysis is to develop a stochastic model for the fluctuating dynamics. Often, those dynamics are well modelled as random jumps between a collection of discrete system states or configurations, x, y, z and so forth. Such a jump process is an appropriate model, for example, for processive molecular motors that progress in discrete steps and for the transport of individual electrons through a quantum dot that generate electrical current. The physical dynamics of this jump process are encoded in a collection of transition rates $r(x,y)$ that specify the probability per unit time to jump from y to x. Then, under fairly mild assumptions, the system's probability density will relax to a unique steady state $\pi(x)$ in the long-time limit.

The dynamics alone, however, are not sufficient to make any thermodynamic inferences. To this end, we now make the central assumption of stochastic thermodynamics and impose physical constraints on the form of the transition rates. The transitions among the system's states are mediated by interactions with individual thermodynamic reservoirs with well-defined (equilibrium) thermodynamic properties, such as temperatures and chemical potentials. The fact that our noisy dynamics is generated by the influence of many equilibrium reservoirs imposes a specific physical constraint on the system's transition rates called local detailed balance, which requires that the asymmetry of transition rates between any pair of

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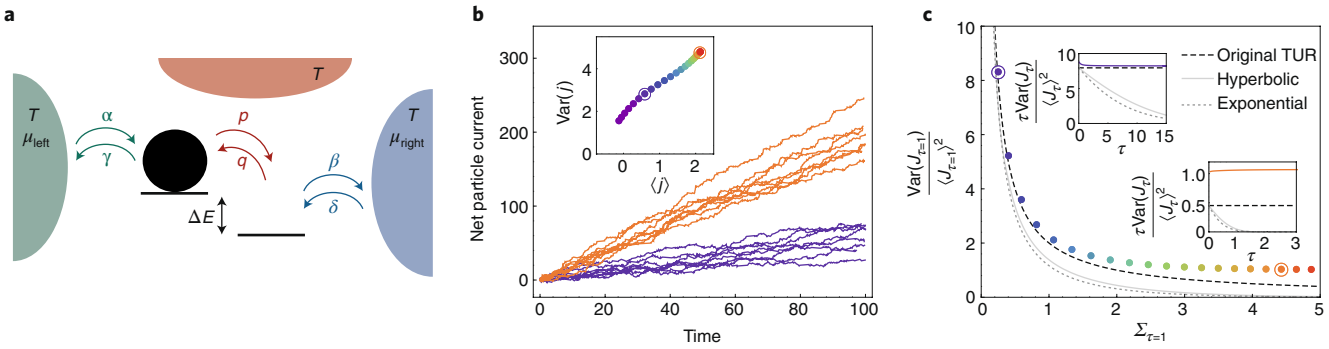


Fig. 1 | Thermodynamic constraints on fluctuations in particle currents. a, Toy model for the non-equilibrium transport of particles between two particle reservoirs at chemical potentials μ_{left} and μ_{right} with temperature T. The system consists of two neighbouring sites that differ in energy by ΔE. Each site may be empty or occupied by a single particle. Particles hop either in/out of particle reservoirs or between sites with rates p, q, α, β, γ, δ as depicted. Stochastic thermodynamics constrains these rates in terms of the equilibrium properties of the reservoirs, T, μ_{left}, μ_{right}, as detailed in Box 1. **b**, Representative time traces for the particle current across the system generated by fixing $\alpha = 2$, $\beta = \gamma = \delta = q = 1$, and then tuning the rate p to vary the irreversibility as measured by the mean dissipation Σ_τ (colour-coded from purple to red). Noise causes the build up of current J_τ to fluctuate both over time and from realization to realization. For low dissipation (purple), the average current grows slowly at rate $\langle j \rangle$ and with it the spread (or variance), yet the variance is large compared with the mean current. At high dissipation (orange), the average current increases with a commensurate increase in variance (inset), yet the uncertainty in the current decreases. **c**, Finite-time ($\tau = 1$) uncertainty in the particle current always exceeds all three forms of the TUR. In the low-dissipation limit the three bounds, which all coincide, are tight. In the high-dissipation limit, the TUR bound becomes weaker as the ultimate constraint to the fluctuations is kinetic, which can be codified with an uncertainty relation for dynamical activity. By plotting the three TUR bounds at relatively short times ($\tau = 1$) we ensure that the dissipation is modest and that the bounds are all similar in magnitude, but as the observation time is increased, the hyperbolic and exponential bounds weaken with a trivial bound of zero in the $\tau \to \infty$ limit (inset).

states is balanced by the non-dimensional change in entropy of the mediating reservoir[1,2]:

$$\sigma(x,y) = \ln \frac{r(x,y)}{r(y,x)} \tag{1}$$

The physical example of Fig. 1a is analysed in Box 1 to explicitly illustrate this link between dynamics and thermodynamics. Roughly speaking, we can think of this entropy production as the energy exhausted to the surroundings in a transition. Thus, to impose more asymmetric rates, thermodynamics requires a steeper energetic penalty.

As the system evolves by hopping between states, it will exchange energy (and sometimes matter) with its surroundings, leading to a production of entropy in accordance with equation (1). Eventually, the system will relax into its non-equilibrium steady state $\pi(x)$, and the average entropy produced Σ_τ during a time window τ will build up at a constant rate

$$\sigma = \Sigma_\tau/\tau = \sum_{x,y} \sigma(x,y) r(x,y) \pi(y) \tag{2}$$

which in some sense represents the thermodynamic cost to maintain the non-equilibrium state.

Dissipation suppresses current fluctuations

Non-equilibrium steady states are characterized not only by the dissipation rate but also by irreversible flows or currents. These currents can physically manifest as the electric current through a resistor, the transport of a molecular motor or the flow of heat down a thermal gradient. In our context of jump processes, each of the physical currents can be expressed as a weighted sum of hops between states[6]:

$$J_\tau = \sum_{x<y} d(x,y) J_\tau(x,y) \tag{3}$$

where $J_\tau(x,y)$ is the net number of transitions from y to x in time τ and $d(x,y)$ is some set of asymmetric jump weights satisfying $d(x,y) = -d(x,y)$. For example, if a state transition represents the transport of electrons in and out of a quantum dot, then the electric current is the hops weighted by the particle's charge. Slightly less trivially, entropy production itself is an important instance of a current with $d(x,y) = \sigma(x,y)$.

Due to the inherent noise in the dynamics, these currents fluctuate when comparing one realized trajectory to the next. We can characterize these fluctuations using their mean $\langle J_\tau \rangle$ and variance $\mathrm{Var}(J_\tau)$ as in Fig. 1b,c. It was recognized that the precision in these steady-state currents — the ratio of variance to mean — can be universally bounded by the entropy production

$$\frac{\mathrm{Var}(J_\tau)}{\langle J_\tau \rangle^2} \geq \frac{2k_B}{\Sigma_\tau} \tag{4}$$

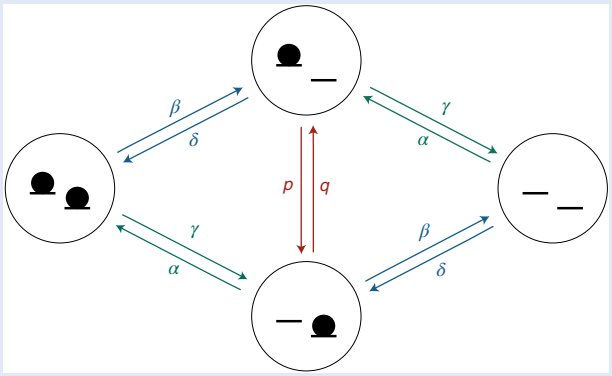
with k_B being Boltzmann's constant[4,7,8]. This observation was proved within the framework of large deviation theory for jump processes using a variational approach that leveraged the statistics of jump processes[5,9,10], an approach that has been adapted to include joint fluctuations of currents[11]. Later, additional analysis[12,13] and alternative derivations[14] that naturally extend to multi-current diffusive dynamics were developed, leveraging information theoretic concepts[15] such as the Cramer–Rao inequality[16,17] or Martingale theory[18].

Equation (4) was named an uncertainty relation since the left-hand side has the interpretation of the uncertainty in the steady-state current observed in a time τ. This uncertainty arises from the stochastic nature of the dynamics, but it is useful to identify two distinct sources of uncertainty.

One source of uncertainty comes from the random fluctuations in the sequence of jumps, including the possibility to backtrack, transitioning back and forth between a pair of states without generating a net build up of current. This type of noise can be alleviated by making the transitions more directed (more asymmetric), which comes with a thermodynamic penalty, cf. equation (1). The overall cost from the directedness of all transitions is the entropy production Σ_τ.

Box 1 | A brief primer on local detailed balance and stochastic thermodynamics

Consider the non-equilibrium system depicted in Fig. 1a. It is useful to visualize the dynamics of this model as a random walk on a graph, where vertices represent configurations and edges allowed transitions:



Note that transitions between vertices need not conserve particle number nor energy. Hence, every transformation of the open system requires the exchange of particles or of energy with the external reservoirs. The local detailed balance condition assumes that exchange occurs with a large equilibrium reservoir.

Let us focus on exchanges with the red thermal reservoir at temperature T. The single particle in the site with high energy E_1 can move to the site with lower energy E_2 with rate p, but in doing so the system will lose energy $\Delta E = E_1 - E_2$. In accordance with the first law, that energy is not really lost, but rather is transferred into the thermal reservoir as heat. Similarly, the uphill step with rate q would require the reservoir to contribute ΔE to the system. Hence, we can shift perspective; rather than ask how probable a right or left hop is, we can equivalently ask how likely it is to observe the red reservoir with an extra ΔE of energy. The probability of energy fluctuations in such an equilibrium reservoir are given by a Boltzmann factor, so

$$\frac{p}{q} = e^{\Delta E/k_B T}$$

Identical logic applies to the exchange of particles with particle reservoirs, those coloured blue and green, so

$$\frac{\alpha}{\gamma} = e^{(\mu_{\text{left}} - E_1)/k_B T} \quad \text{and} \quad \frac{\beta}{\delta} = e^{-(\mu_{\text{right}} - E_2)/k_B T}$$

with μ_{left} and μ_{right} the chemical potentials of the left (green) and right (blue) particle reservoirs. We recognize the terms in all three exponents as the unitless entropy increase of the reservoir on the transfer of an additional unit of energy (and an additional particle), in agreement with the general local detailed balance statement in equation (1).

By construction, each environmental reservoir is assumed so large that interactions with the system cannot alter its equilibrium state, so energy (and particles) is exchanged reversibly. Even though each transition is near equilibrium in this sense, the system as a whole can be quite far from equilibrium if the various reservoirs have very dissimilar equilibrium states. In that case, cyclical probability fluxes on the graph emerge. Each cycle returns the system to its original state while shuttling particles and energy among the reservoirs. Notably, the local detailed balance condition requires that the relative probability of traversing a cycle clockwise and anticlockwise is determined by the entropy production in all the reservoirs over the course of a cycle. For example:

$$\ln \frac{\text{prob}\left(p\downarrow \xrightarrow{\alpha} \xrightarrow{\beta}\right)}{\text{prob}\left(q\uparrow \xrightarrow{\gamma} \xrightarrow{\delta}\right)} = \ln\frac{\alpha}{\gamma} + \ln\frac{\beta}{\delta} + \ln\frac{p}{q} = \frac{\mu_{\text{left}}}{k_B T} - \frac{\mu_{\text{right}}}{k_B T}$$

Thus, we have seen that when the dynamics of a physical system are mediated by equilibrium reservoirs, the kinetic rates cannot be independent, but must be interrelated through the thermodynamic properties of the environment as captured by local detailed balance.

The other source of noise relates, not to the entropy production, but to the statistics of the transition times. Even with a fixed sequence of jumps, the time between jumps is random. The fluctuations in jump times are inherent to continuous-time dynamics and cannot be avoided by making the process more dissipative[19–21]. Indeed, current fluctuations in discrete-time stochastic processes can be smaller than their continuous-time counterparts because discrete-time dynamics lacks the jump-time noise[20,22,23].

In practice

Uncertainty relations have been verified in numerous scenarios, both within specific models[24–32] as well as experimentally[7]. The most interesting applications, however, take a step beyond validation of the inequality and instead use it as the basis for inference[8,33].

A good example of such an application comes from the analysis in ref. [34] of the thermodynamic efficiency of a processive molecular motor. Molecular motors driven by the chemical potential gradient $\Delta\mu$ for ATP hydrolysis are designed to pull cargo against a mechanical force f at velocity v while consuming ATP at a rate $\dot{N}_{\text{ATP}}$. The thermodynamic efficiency is the ratio of the work done against the mechanical force vf divided by the chemical work supplied by the ATP $\dot{N}_{\text{ATP}}\Delta\mu$: $\eta = vf/\dot{N}_{\text{ATP}}\Delta\mu$. This engine converts chemical work to mechanical work and in this case the second law only limits the efficiency to $\eta \leq 1$, which is not terribly informative. Using the motor velocity as the current, the uncertainty relation imposes a tighter bound given knowledge of the motor's velocity fluctuations

$$\eta \leq \frac{1}{1 + \nu k_B T/\text{Var}(v)f} \tag{5}$$

As noted in ref. [34], this inequality further allows one to obtain thermodynamic information — a bound on the efficiency — purely from a kinematic measurement of the motion of the motor, which can be easier to measure experimentally than direct measurement of the ATP consumption rate. In ref. [35], that efficiency bound was studied as a function of the load force applied to a kinesin motor.

Extending to new classes of dynamics

The TUR in equation (4) applies to jump or diffusion processes evolving in continuous time with time-independent non-equilibrium drives that do not change sign under time reversal. Those conditions exclude some notable classes of dynamics: driven systems subject to a time-dependent driving protocol[36], quantum non-equilibrium dynamics[37–39] and motion involving quantities such as momenta or magnetic fields[40–43]. It was quickly realized that equation (4) could be violated by relaxing any one of these assumptions.

However, this failure inspired the development of an extended form of thermodynamic uncertainty relation

$$\frac{\mathrm{Var}(J_\tau)}{\langle J_\tau\rangle^2} \geq f\left(\frac{\Sigma_\tau}{k_\mathrm{B}}\right) \tag{6}$$

where f is a function of only the dissipation. The original TUR, equation (4), takes $f(x) = 2/x$; TUR extensions trade broader applicability for a weaker f.

From the finite-time fluctuation theorem. Rather than focus case by case on different types of dynamics, one can consider the consequences of symmetry on current fluctuations. Namely, the joint fluctuations of any current and entropy production verify a fluctuation theorem for many types of non-equilibrium models, including quantum dynamics, time-symmetric periodic driving and underdamped Brownian motion.

Starting from such a fluctuation theorem, in ref. [44] it was demonstrated that current fluctuations could be bounded by an exponential bound of the form $f_\mathrm{e}(x) = 2/(\mathrm{e}^x - 1)$. Shortly thereafter, under nearly the same conditions, the tightest bound implied by the fluctuation theorem symmetry was shown to have a hyperbolic form $f_\mathrm{h}(x) = \mathrm{csch}^2(g^{-1}(x/2))$, where $g(y) = y\tanh(y)$ (ref. [45]). Since the hyperbolic bound holds for a broad class of finite-time trajectories, one might expect it to supersede the original TUR with $f(x) = 2/x$. The hyperbolic inequality, however, is weaker; jump process current fluctuations are more restricted than the fluctuation theorem symmetry alone could predict. This weakness could be especially detrimental if one aims to use the TUR as a basis to infer entropy production from current fluctuations[46]: a weaker bound leads to poorer inference.

Crucially, the difference between the uncertainty relations becomes especially stark in the limit of long trajectories, a limit for which the hyperbolic and exponential inequalities lose their power, as observed in Fig. 1c.

The long-time limit. To see the differing long-time behaviour, consider first the $\tau \to \infty$ limit of the finite-time TUR, equation (4). In actuality, this long-time limit was observed and proven before the finite-time result was known, but we have inverted the chronology to highlight how one result follows from the other. At long times, systems in non-equilibrium steady states are constantly producing entropy with rate $\sigma = \lim_{\tau\to\infty} \Sigma_\tau/\tau$. In addition, any integrated current grows with a fixed rate $\langle j\rangle = \lim_{\tau\to\infty}\langle J_\tau\rangle/\tau$ and its fluctuations diffuse with $\mathrm{Var}(j) = \lim_{\tau\to\infty} \mathrm{Var}(J_\tau)/\tau$. The TUR, equation (4), then predicts a non-trivial bound on the long-time fluctuations[4,5]

$$\lim_{\tau\to\infty} \frac{\tau\mathrm{Var}(J_\tau)}{\langle J_\tau\rangle^2} = \frac{\mathrm{Var}(j)}{\langle j\rangle^2} \geq \frac{2k_\mathrm{B}}{\sigma} \tag{7}$$

In analogy, one might like to convert finite-time results of the form given in equation (6) into long-time inequalities with the right-hand side replaced by some function of the entropy production rate σ. The aim again is to uncover inequalities reliant only on fluctuation theorems, which would remain valid even for classes of dynamical processes for which equation (7) breaks down. The natural candidate is to use the $\tau \to \infty$ limit of the finite-time bounds f_e and f_h, but both limits give only the trivial long-time inequality $\mathrm{Var}(j)/\langle j\rangle^2 \geq 0$. Though the fluctuation theorem symmetry was sufficient to bound finite time current fluctuations $\mathrm{Var}(J_\tau)/\langle J_\tau\rangle^2$ in terms of Σ_τ, it does not yield a similar constraint on $\mathrm{Var}(j)/\langle j\rangle^2$ in terms of the entropy production rate σ.

Despite this limitation, a non-trivial bound does exist for time-symmetric periodic driving, a situation for which equation (7) is not generally valid. Using a large-deviation variational approach, the current fluctuations per period τ in the long-time limit was bound by a modified exponential[23]

$$\frac{\mathrm{Var}(j)}{\langle j\rangle^2} \geq \frac{2\tau}{e^{\sigma\tau/k_\mathrm{B}} - 1} = \tau f_\mathrm{e}(\sigma\tau/k_\mathrm{B}) \tag{8}$$

where $\sigma\tau$ is the average entropy produced in one period. It is suggestive that the bound involves the same exponential function f_e appearing in the finite-time results. That shared structure hints that a form of equation (8) built around f_h may also hold for time-symmetric periodic driving. It remains an open problem whether one can develop these and other bounds on the long-time current fluctuations using only symmetry considerations like the fluctuation theorem.

Breaking time-reversal symmetry. The finite-time and long-time results discussed thus far all apply to dynamics with time-reversal symmetry. To include driving that breaks time-reversal symmetry, such as magnetic fields, time-asymmetric external protocols or even feedback, we need a slight modification of what we mean by an uncertainty relation.

Here, the action of time-reversal alters the physical nature of the process, for example, a magnetic field changes directions. So in this scenario, we can consider the current fluctuations in the original process J_τ and the time-reversed process (say with the magnetic field flipped), $\tilde{J}_\tau$. Then the time-symmetrized hysteric current, $J_\tau + \tilde{J}_\tau$, verifies the same finite-time uncertainty relations[47,48]. That symmetrizing is required appears to reinforce the intimate relation between time-reversal symmetry and the TURs, but again restricted to only finite-time fluctuations. Extensions to long-time results like equation (8) would be especially beneficial for investigating the efficiencies of driven periodic heat engines, whose external driving is rarely restricted to being time symmetric.

Going beyond dissipative bounds on current fluctuations

We have focused on thermodynamic uncertainty relations that constrain current fluctuations by some function of the average entropy production rate. The methods used in their derivation turn out to be quite powerful and general, allowing one to generate a diversity of TUR-like relations for the precision of other variables besides currents. They have already been applied to derive various trade-off relations for quantities such as activity[21,49], first passage times[49,50] and equilibrium order parameters[51]. While some of these fluctuation bounds also involve the entropy production rate, others constrain fluctuations by kinetic properties of the dynamics like the average activity[52–54], by measures that depend on the topology of the state space[41,55], or by including the dynamic sensitivity to driving allowing one to constrain the efficiency of driven periodic heat engines[56].

Each such inequality has advantages and disadvantages, both in conceptual insight and in practical implementation. Depending on system parameters and the precision of measurement, each bound offers differing constraints on the magnitude of fluctuations. We envision that by combining a variety of such fluctuation bounds for differing observables one can place useful constraints on model parameters and perhaps even aid in model selection. Such an insight could be especially valuable for biological systems, where it is challenging to infer precise microscopic mechanisms.

What's next?

All this work has lead to a collection of relations derived using a zoo of techniques that are valid for a heterogeneous mixture of scenarios. This diversity is both exciting and daunting. In fact, the current situation is reminiscent of the early history in the development of the fluctuation relations: numerous seemingly distinct predictions had been made based on different physical assumptions about the dynamics, for example, non-equilibrium steady-state fluctuations

versus finite-time work protocols. However, it was later recognized that all these predictions were variations of a single fluctuation relation and therefore could be rationalized within a single coherent approach. The lesson is that universal thermodynamic statements tend not to be highly sensitive to precise modelling assumptions.

While we do not expect a single master TUR, it would be desirable to have an organized hierarchy of inequalities with precisely delineated regions of validity. Such a broad picture would be especially valuable for extracting information from experimental measurements, since it would allow one to coherently weave together various relations based on any specific knowledge of the dynamics.

Non-equilibrium statistical thermodynamics has been rapidly unravelling thermodynamic connections and symmetries buried in the fluctuations of non-equilibrium systems. Here, we have taken a look at one recent class of such predictions. Though looking further forward, it is tempting to hope that there are many more of these types of trade-offs that quantitatively describe how thermodynamics dictates non-equilibrium structure and function.

For example, one of the oldest themes in equilibrium statistical physics is the connection between fluctuations and response. The TURs have taught us about fundamental non-equilibrium restrictions on certain classes of dynamical fluctuations, which naturally leads to the question of whether similar types of restrictions apply to dynamical response[15,57]. We anticipate that there remains much more to understand about the thermodynamic connections between far-from-equilibrium fluctuations and response.

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