

Figure 1 | A mechanism of redundancy. **a**, The premotor cortex regions in each hemisphere of the mouse brain, which are connected by neurons (double-headed arrows), produce activity that prepares the animal to move its tongue left or right. Li *et al.*¹ genetically engineered mice such that blue light could temporarily block neuronal activity in these regions, erasing information about the intended direction of movement. If information is erased in one hemisphere, it is quickly restored. **b**, By contrast, if information is erased in both hemispheres, it is not restored.

known as redundancy. Specifically, they tested whether the two premotor cortices of the mouse brain act redundantly to prepare the animal to lick with its tongue in a particular direction, which it has been taught will lead to a reward of water. The authors briefly blocked the activity of premotor neurons in one hemisphere and observed that information about intended licking direction was quickly restored (Fig. 1a). However, if they silenced neurons in both hemispheres in this way, the information was not restored, and so the animal licked left or right at random (Fig. 1b).

These results indicate that, during single-hemisphere silencing, fault tolerance is provided by the unmodified hemisphere. To test this back-up system more directly, the researchers severed the connections between the two hemispheres. When neurons in one hemisphere were silenced in this setting, the information about intended licking direction was not restored.

Next, Li *et al.* constructed computational network models of neurons in two interacting hemispheres to study how connectivity between the two brain regions enables fault tolerance. In these models, as in the experimental setting, information about movement direction was restored after neuronal silencing in one hemisphere. Together with the experimental evidence, these data suggest that each hemisphere helps the other to restore information about planned movement direction.

Perhaps the most interesting finding in this study is that, after silencing neurons in one hemisphere, not all aspects (called dimensions) of the perturbed neural activity recovered equally. Li and colleagues found that the neural activity that enabled maximal differentiation

between left and right licks recovered rapidly. By contrast, other dimensions of neural activity that were not relevant to the task did not always recover. Thus, there was preferential recovery of the dimension that was needed for the animal to succeed at the licking task.

The current study involved both hemispheres controlling a single effector, the tongue. An open question is how these findings apply to brain functions that predominantly involve a single hemisphere, such as control over reaching with one arm. As the authors point out, one possibility is that there are redundant subcircuits within a hemisphere, perhaps spread across multiple brain areas, working together to provide fault tolerance.

Li *et al.* perturbed neural activity using an

optogenetic technique, in which the activity of neurons that harbour light-sensitive ion channels can be modulated using light. This approach allows the silencing or activation of many neurons in unison. To further understand the fault-tolerant properties of neural circuits, more-flexible methods that allow selective activation and silencing of different groups of neurons at different times are needed. Such methods would permit testing of the robustness of a neural circuit to different patterns of perturbation, including those that mimic the random signal disturbances, known as noise, that are a part of normal neuronal signalling³.

The current work demonstrates the power of perturbing neural activity in combination with multidimensional analysis of the activity of a neural population⁴. By perturbing neural activity in different ways and observing how it recovers, we should be able to gain further insights into fundamental network-level mechanisms that support brain functions⁵. Advances in methods for perturbing and recording neural activity, for analysing population-wide neural activity and for network modelling are rapidly making such studies possible. ■

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MATHEMATICAL PHYSICS

Glitches in time

A mathematical technique has now been developed that reveals the underlying dynamics of time-dependent data collected with extreme temporal uncertainty, without using additional, costly instrumentation. SEE LETTER P.471

CHARLOTTE A. L. HALEY

Many of today's scientific questions require the reconstruction of accurate histories from data collected with uncertainty in the temporal or spatial measurement process. Examples include the systematic errors in timing or spacing seen in measurements of astronomical

time series collected at uneven intervals^{1,2}; in determinations of global climate history from concentrations of gas extracted from bubbles in ice cores drilled in the Antarctic³; and in deductions of the proximity of far-away galaxies when the observed light is bent by gravitational lensing⁴. On page 471 of this issue, Fung *et al.*⁵ report a mathematical method that allowed them to analyse data with uneven temporal

spacing or samples that appeared out of order.

Free-electron lasers allow the early stages of ultrafast chemical reactions to be studied with molecular precision^{6,7}. Fung *et al.* used X-ray free-electron lasers to investigate a fundamental chemical process: the photoionization of nitrogen molecules, whereby the nitrogen ions N_2^+ and N_2^{2+} are created after photon absorption by molecular nitrogen (N_2). The ionization plays out incredibly quickly, over a period of several hundred femtoseconds (1 fs is 10^{-15} seconds).

The authors used an infrared pulse to trigger photoionization and an X-ray pulse to probe the process, capturing snapshots using a spectrometer with a ‘shutter speed’ of less than 100 fs. Unfortunately, thermal noise in the instrument introduces timing uncertainty that can exceed 280 fs (ref. 7). This temporal uncertainty, or jitter, makes it difficult to measure quantities such as the vibrating frequencies of the molecular system.

Fung *et al.* used a mathematical technique known as nonlinear Laplacian spectral analysis (NLSA) to recover the true dynamics underlying these snapshots (Fig. 1). In this technique, the data are embedded in a multi-dimensional space characterized by Laplacian functions, which can represent turbulent or intermittent structure in the data. The technique is nonlinear because the data are mapped to a curved surface. The term ‘spectral’ is used because, just as a prism separates white light into a spectrum of long to short wavelengths, NLSA decomposes the snapshots into their constituent time and space components (known as chronograms and topograms, respectively), arranged from strongest (the largest contributors to the signal) to weakest (the smallest contributors; Fig. 1b,c). The authors’ key observation is that the chronograms are robust to jitter. In other words, the data points in the chronograms are uniformly spaced in time, which means that it is, in principle, possible to reconstruct the original data without jitter by recombining the modes.

However, NLSA does not allow such a reconstruction except in simple examples, because it requires a huge number of unknown parameters to be estimated. But reconstruction is not the goal. Instead, the quantities of interest can be observed directly by looking at the strongest ‘modes’ obtained from NLSA — these modes are derived mathematically from the chronograms and topograms, and describe the essential properties of the nitrogen system. One of the modes reveals an especially interesting result: molecular nitrogen vibrates with three previously unobserved frequencies. These are in the 16–24-fs range — much shorter than those observed in any preceding experiment, but consistent with predictions from quantum mechanical theory.

Aside from this important application to quantum molecular physics, the theory proposed by Fung *et al.* has profound implications

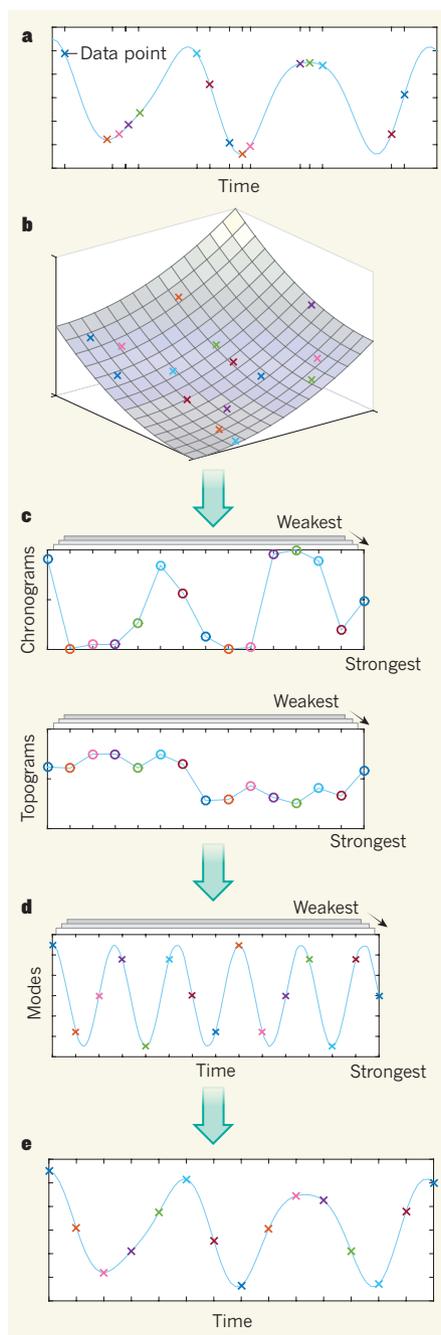


Figure 1 | A mathematical process for analysing space-time data. Fung *et al.*⁵ studied the vibrations and break-up of nitrogen molecules in response to a single infrared trigger pulse and a probing X-ray pulse. **a**, The collected space-time data were unevenly distributed in time and sometimes in the wrong order (data from a single spatial coordinate are shown). **b**, **c**, To extract the underlying temporal dynamics, the authors embedded the data in a five-dimensional nonlinear space (**b**, three dimensions are shown, for simplicity), then decomposed the data into a series of time and space components (**c**, chronograms and topograms, respectively), organized from strongest to weakest. **d**, These components can be used to construct modes that describe the essential properties of the nitrogen system and have uniform time spacing. **e**, In principle, the original data without timing errors can be reconstructed from a combination of these modes.

for signal processing and spatiotemporal statistics. Techniques for the spectral analysis of time series or spatial data involving uneven sampling or missing data, both with known and unknown timestamps, have been sought since at least the early 1980s (refs. 2,3,8,9). It is remarkable that, in the molecular-nitrogen experiment, the authors can resolve the vibrational modes to about 1 fs spacing. However, an expression for the reduction in temporal uncertainty achieved after application of this technique is desirable. Another question is whether NLSA can return a uniform result if signals are systematically bunched in time. And finally, if NLSA is applicable to unevenly timed samples, it ought to be applicable to unevenly spaced samples in one spatial dimension — but are there nonlinear embeddings that can extend this result into higher dimensions?

The authors verified their observations by numerical simulation, but mathematical rigour and theoretical formalism for the temporal uniformity of the chronogram components are still lacking. Moreover, the presented formulation may still be overly complex. In particular, the authors show that a single cosine curve, sampled with jitter, can be recovered without the need for a nonlinear approach. Given that this simple cosine example underlies all conventional spectrum analysis¹⁰, is there a simpler formulation that does not require the complex machinery of NLSA but still possesses the property of time uniformity in the result? What is the simplest, most basic working example of such a process? This work opens the door to many interesting questions. ■

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CORRECTION

In the News & Views article ‘Physics: Quantum problems solved through games’ by Sabrina Maniscalco (*Nature* **532**, 184–185; 2016), reference 7 was incorrect. The correct reference is <https://www.scienceathome.org/games/quantum-moves/game>