

Interrogating theoretical models of neural computation with emergent property inference

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¹ 1 Abstract

² A cornerstone of theoretical neuroscience is the circuit model: a system of equations that captures
³ a hypothesized neural mechanism. Such models are valuable when they give rise to an experimen-
⁴ tally observed phenomenon – whether behavioral or a pattern of neural activity – and thus can
⁵ offer insights into neural computation. The operation of these circuits, like all models, critically
⁶ depends on the choice of model parameters. A key step is then to identify the model parameters
⁷ consistent with observed phenomena: to solve the inverse problem. In this work, we present a
⁸ novel technique, emergent property inference (EPI), that brings the modern probabilistic modeling
⁹ toolkit to theoretical neuroscience. When theorizing circuit models, theoreticians predominantly
¹⁰ focus on reproducing computational properties rather than a particular dataset. Our method uses
¹¹ deep neural networks to learn parameter distributions with these computational properties. This
¹² methodology is introduced through a motivational example inferring conductance parameters in a
¹³ circuit model of the stomatogastric ganglion. Then, with recurrent neural networks of increasing
¹⁴ size, we show that EPI allows precise control over the behavior of inferred parameters, and that
¹⁵ EPI scales better in parameter dimension than alternative techniques. In the remainder of this
¹⁶ work, we present novel theoretical findings gained through the examination of complex parametric
¹⁷ structure captured by EPI. In a model of primary visual cortex, we discovered how connectivity
¹⁸ with multiple inhibitory subtypes shapes variability in the excitatory population. Finally, in a
¹⁹ model of superior colliculus, we identified and characterized two distinct regimes of connectivity

20 that facilitate switching between opposite tasks amidst interleaved trials, characterized each regime
21 via insights afforded by EPI, and found conditions where these circuit models reproduce results
22 from optogenetic silencing experiments. Beyond its scientific contribution, this work illustrates
23 the variety of analyses possible once deep learning is harnessed towards solving theoretical inverse
24 problems.

25 2 Introduction

26 The fundamental practice of theoretical neuroscience is to use a mathematical model to understand
27 neural computation, whether that computation enables perception, action, or some intermediate
28 processing. A neural circuit is systematized with a set of equations – the model – and these
29 equations are motivated by biophysics, neurophysiology, and other conceptual considerations [1–5].

30 The function of this system is governed by the choice of model *parameters*, which when configured
31 in a particular way, give rise to a measurable signature of a computation. The work of analyzing
32 a model then requires solving the inverse problem: given a computation of interest, how can we
33 reason about the distribution of parameters that give rise to it? The inverse problem is crucial for
34 reasoning about likely parameter values, uniquenesses and degeneracies, and predictions made by
35 the model [6–8].

36 Ideally, one carefully designs a model and analytically derives how computational properties deter-
37 mine model parameters. Seminal examples of this gold standard include our field’s understanding
38 of memory capacity in associative neural networks [9], chaos and autocorrelation timescales in ran-
39 dom neural networks [10], central pattern generation [11], the paradoxical effect [12], and decision
40 making [13]. Unfortunately, as circuit models include more biological realism, theory via analytical
41 derivation becomes intractable. Absent this analysis, statistical inference offers a toolkit by which
42 to solve the inverse problem by identifying, at least approximately, the distribution of parameters
43 that produce computations in a biologically realistic model [14–19].

44 Statistical inference, of course, requires quantification of the sometimes vague term *computation*.
45 In neuroscience, two perspectives are dominant. First, often we directly use an *exemplar dataset*:
46 a collection of samples that express the computation of interest, this data being gathered either
47 experimentally in the lab or from a computer simulation. Though a natural choice given its con-
48 nection to experiment [20], some drawbacks exist: these data are well known to have features
49 irrelevant to the computation of interest [21–23], confounding inferences made on such data. Re-

50 lated to this point, use of a conventional dataset encourages conventional data likelihoods or loss
51 functions, which focus on some global metric like squared error or marginal evidence, rather than
52 the computation itself.

53 Alternatively, researchers often quantify an *emergent property* (EP): a statistic of data that directly
54 quantifies the computation of interest, wherein the dataset is implicit. While such a choice may
55 seem esoteric, it is not: the above “gold standard” examples [9–13] all quantify and focus on
56 some derived feature of the data, rather than the data drawn from the model. An emergent
57 property is of course a dataset by another name, but it suggests different approach to solving
58 the same inverse problem: here we directly specify the desired emergent property – a statistic
59 of data drawn from the model – and the value we wish that property to have, and we set up
60 an optimization program to find the distribution of parameters that produce this computation.
61 This statistical framework is not new: it is intimately connected to the literature on approximate
62 bayesian computation [24–26], parameter sensitivity analyses [27–30], maximum entropy modeling
63 [31–33], and approximate bayesian inference [34, 35]; we detail these connections in Section 5.1.1.

64 The parameter distributions producing a computation may be curved or multimodal along vari-
65 ous parameter axes and combinations. It is by quantifying this complex structure that emergent
66 property inference offers scientific insight. Traditional approximation families (e.g. mean-field or
67 mixture of gaussians) are limited in the distributional structure they may learn. To address such re-
68 strictions on expressivity, advances in machine learning have used deep probability distributions as
69 flexible approximating families for such complicated distributions [36, 37] (see Section 5.1.2). How-
70 ever, the adaptation of deep probability distributions to the problem of theoretical circuit analysis
71 requires recent developments in deep learning for constrained optimization [38], and architectural
72 choices for efficient and expressive deep generative modeling [39, 40]. We detail our method, which
73 we call emergent property inference (EPI) in Section 3.2.

74 Equipped with this method, we demonstrate the capabilities of EPI and present novel theoretical
75 findings from its analysis. First, we show EPI’s ability to handle biologically realistic circuit models
76 using a five-neuron model of the stomatogastric ganglion [41]: a neural circuit whose parametric
77 degeneracy is closely studied [42]. Then, we show EPI’s scalability to high dimensional parameter
78 distributions by inferring connectivities of recurrent neural networks that exhibit stable, yet ampli-
79 fied responses – a hallmark of neural responses throughout the brain [43–45]. In a model of primary
80 visual cortex [46, 47], EPI reveals how the recurrent processing across different neuron-type popu-
81 lations shapes excitatory variability: a finding that we show is analytically intractable. Finally, we

82 investigated the possible connectivities of a superior colliculus model that allow execution of differ-
83 ent tasks on interleaved trials [48]. EPI discovered a rich distribution containing two connectivity
84 regimes with different solution classes. We queried the deep probability distribution learned by
85 EPI to produce a mechanistic understanding of neural responses in each regime. Intriguingly, the
86 inferred connectivities of each regime reproduced results from optogenetic inactivation experiments
87 in markedly different ways. These theoretical insights afforded by EPI illustrate the value of deep
88 inference for the interrogation of neural circuit models.

89 **3 Results**

90 **3.1 Motivating emergent property inference of theoretical models**

91 Consideration of the typical workflow of theoretical modeling clarifies the need for emergent prop-
92 erty inference. First, one designs or chooses an existing circuit model that, it is hypothesized,
93 captures the computation of interest. To ground this process in a well-known example, consider
94 the stomatogastric ganglion (STG) of crustaceans, a small neural circuit which generates multiple
95 rhythmic muscle activation patterns for digestion [49]. Despite full knowledge of STG connectivity
96 and a precise characterization of its rhythmic pattern generation, biophysical models of the STG
97 have complicated relationships between circuit parameters and computation [15, 42].

98 A subcircuit model of the STG [41] is shown schematically in Figure 1A. The fast population (f_1
99 and f_2) represents the subnetwork generating the pyloric rhythm and the slow population (s_1 and
100 s_2) represents the subnetwork of the gastric mill rhythm. The two fast neurons mutually inhibit
101 one another, and spike at a greater frequency than the mutually inhibiting slow neurons. The
102 hub neuron couples with either the fast or slow population, or both depending on modulatory
103 conditions. The jagged connections indicate electrical coupling having electrical conductance g_{el} ,
104 smooth connections in the diagram are inhibitory synaptic projections having strength g_{synA} onto
105 the hub neuron, and $g_{synB} = 5nS$ for mutual inhibitory connections. Note that the behavior of this
106 model will be critically dependent on its parameterization – the choices of conductance parameters
107 $\mathbf{z} = [g_{el}, g_{synA}]$.

108 Second, once the model is selected, one must specify what the model should produce. In this STG
109 model, we are concerned with neural spiking frequency, which emerges from the dynamics of the
110 circuit model (Fig. 1B). An emergent property studied by Gutierrez et al. is the hub neuron firing
111 at an intermediate frequency between the intrinsic spiking rates of the fast and slow populations.

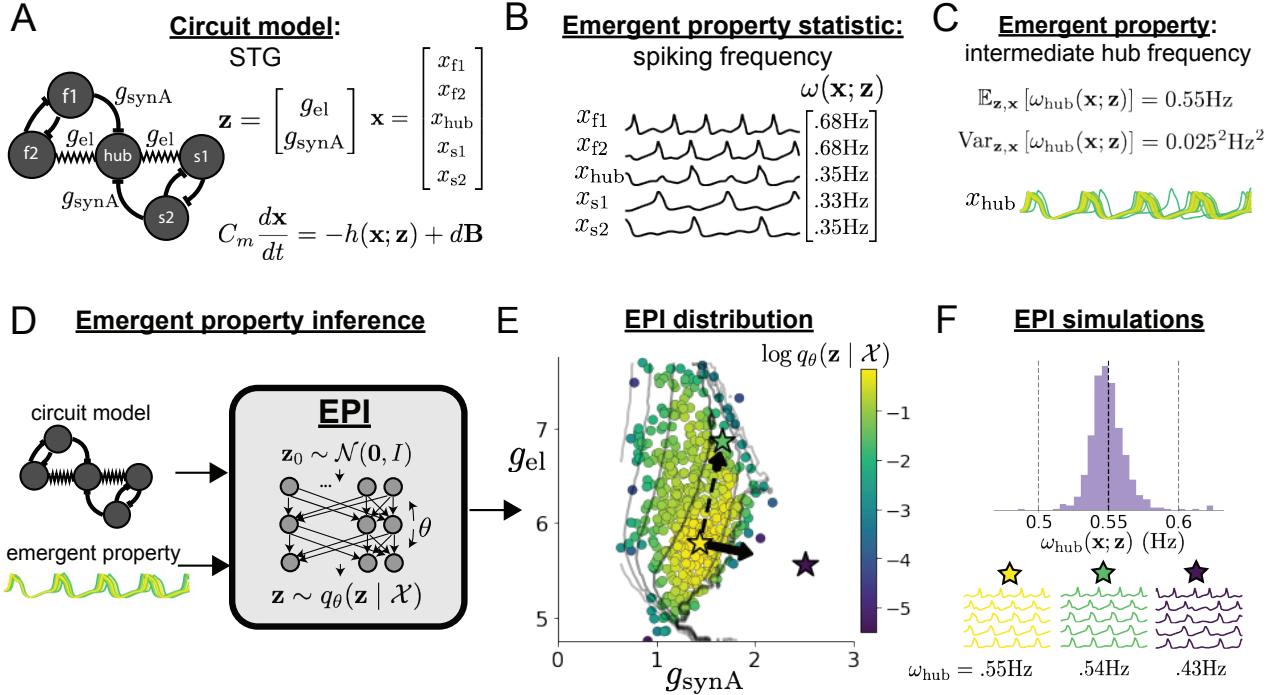


Figure 1: Emergent property inference in the stomatogastric ganglion. **A.** Conductance-based subcircuit model of the STG. **B.** Spiking frequency $\omega(\mathbf{x}; \mathbf{z})$ is an emergent property statistic. Simulated at $g_{el} = 4.5\text{nS}$ and $g_{synA} = 3\text{nS}$. **C.** The emergent property of intermediate hub frequency. Simulated activity traces are colored by log probability of generating parameters in the EPI distribution (Panel E). **D.** For a choice of circuit model and emergent property, EPI learns a deep probability distribution of parameters \mathbf{z} . **E.** The EPI distribution producing intermediate hub frequency. Samples are colored by log probability density. Contours of hub neuron frequency error are shown at levels of .525, .53,575 Hz (dark to light gray away from mean). Dimension of sensitivity \mathbf{v}_1 (solid arrow) and robustness \mathbf{v}_2 (dashed arrow). **F** (Top) The predictions of the EPI distribution. The black and gray dashed lines show the mean and two standard deviations according the emergent property. (Bottom) Simulations at the starred parameter values.

112 This emergent property (EP) is shown in Figure 1C at an average frequency of 0.55Hz. To be
113 precise, we define intermediate hub frequency not strictly as 0.55Hz, but frequencies of moderate
114 deviation from 0.55Hz between the fast (.35Hz) and slow (.68Hz) frequencies.

115 Third, the model parameters producing the emergent property are inferred. By precisely quantify-
116 ing the emergent property of interest as a statistical feature of the model, we use emergent property
117 inference (EPI) to condition directly on this emergent property. Before presenting technical details
118 (in the following section), let us understand emergent property inference schematically. EPI (Fig.
119 1D) takes, as input, the model and the specified emergent property, and as its output, returns
120 the parameter distribution (Fig. 1E). This distribution – represented for clarity as samples from
121 the distribution – is a parameter distribution constrained such that the circuit model produces the
122 emergent property. Once EPI is run, the returned distribution can be used to efficiently gener-
123 ate additional parameter samples. Most importantly, the inferred distribution can be efficiently
124 queried to quantify the parametric structure that it captures. By quantifying the parametric struc-
125 ture governing the emergent property, EPI informs the central question of this inverse problem:
126 what aspects or combinations of model parameters have the desired emergent property?

127 3.2 Emergent property inference via deep generative models

128 EPI formalizes the three-step procedure of the previous section with deep probability distributions
129 [36, 37]. First, as is typical, we consider the model as a coupled set of noisy differential equations.
130 In this STG example, the model activity (or state) $\mathbf{x} = [x_{f1}, x_{f2}, x_{hub}, x_{s1}, x_{s2}]$ is the membrane
131 potential for each neuron, which evolves according to the biophysical conductance-based equation:

$$C_m \frac{d\mathbf{x}(t)}{dt} = -h(\mathbf{x}(t); \mathbf{z}) + d\mathbf{B} \quad (1)$$

132 where $C_m = 1\text{nF}$, and \mathbf{h} is a sum of the leak, calcium, potassium, hyperpolarization, electrical, and
133 synaptic currents, all of which have their own complicated dependence on activity \mathbf{x} and parameters
134 $\mathbf{z} = [g_{el}, g_{synA}]$, and $d\mathbf{B}$ is white gaussian noise [41] (see Section 5.2.1 for more detail).

135 Second, we determine that our model should produce the emergent property of “intermediate hub
136 frequency” (Figure 1C). We stipulate that the hub neuron’s spiking frequency – denoted by statistic
137 $\omega_{hub}(\mathbf{x})$ – is close to a frequency of 0.55Hz, between that of the slow and fast frequencies. Mathe-
138 matically, we define this emergent property with two constraints: that the mean hub frequency is
139 0.55Hz,

$$\mathbb{E}_{\mathbf{z}, \mathbf{x}} [\omega_{hub}(\mathbf{x}; \mathbf{z})] = 0.55 \quad (2)$$

140 and that the variance of the hub frequency is moderate

$$\text{Var}_{\mathbf{z}, \mathbf{x}} [\omega_{\text{hub}}(\mathbf{x}; \mathbf{z})] = 0.025^2. \quad (3)$$

141 In the emergent property of intermediate hub frequency, the statistic of hub neuron frequency is
142 an expectation over the distribution of parameters \mathbf{z} and the distribution of the data \mathbf{x} that those
143 parameters produce. We define the emergent property \mathcal{X} as the collection of these two constraints.
144 In general, an emergent property is a collection of constraints on statistical moments that together
145 define the computation of interest.

146 Third, we perform emergent property inference: we find a distribution over parameter configura-
147 tions \mathbf{z} of models that produce the emergent property; in other words, they satisfy the constraints
148 introduced in Equations 2 and 3. This distribution will be chosen from a family of probability
149 distributions $\mathcal{Q} = \{q_{\theta}(\mathbf{z}) : \theta \in \Theta\}$, defined by a deep neural network [36, 37] (Figure 1D, EPI box).
150 Deep probability distributions map a simple random variable \mathbf{z}_0 (e.g. an isotropic gaussian) through
151 a deep neural network with weights and biases θ to parameters $\mathbf{z} = g_{\theta}(\mathbf{z}_0)$ of a suitably compli-
152 cated distribution (see Section 5.1.2 for more details). Many distributions in \mathcal{Q} will respect the
153 emergent property constraints, so we select the most random (highest entropy) distribution, which
154 also means this approach is equivalent to bayesian variational inference (see Section 5.1.6). In EPI
155 optimization, stochastic gradient steps in θ are taken such that entropy is maximized, and the
156 emergent property \mathcal{X} is produced (see Section 5.1). We then denote the inferred EPI distribution
157 as $q_{\theta}(\mathbf{z} | \mathcal{X})$, since the structure of the learned parameter distribution is determined by weights
158 and biases θ , and this distribution is conditioned upon emergent property \mathcal{X} .

159 The structure of the inferred parameter distributions of EPI can be analyzed to reveal key infor-
160 mation about how the circuit model produces the emergent property. As probability in the EPI
161 distribution decreases away from the mode of $q_{\theta}(\mathbf{z} | \mathcal{X})$ (Fig. 1E yellow star), the emergent prop-
162 erty deteriorates. Perturbing \mathbf{z} along a dimension in which $q_{\theta}(\mathbf{z} | \mathcal{X})$ changes little will not disturb
163 the emergent property, making this parameter combination *robust* with respect to the emergent
164 property. In contrast, if \mathbf{z} is perturbed along a dimension with strongly decreasing $q_{\theta}(\mathbf{z} | \mathcal{X})$,
165 that parameter combination is deemed *sensitive* [27, 30]. By querying the second order derivative
166 (Hessian) of $\log q_{\theta}(\mathbf{z} | \mathcal{X})$ at a mode, we can quantitatively identify how sensitive (or robust) each
167 eigenvector is by its eigenvalue; the more negative, the more sensitive and the closer to zero, the
168 more robust (see Section 5.2.4). Indeed, samples equidistant from the mode along these dimensions
169 of sensitivity (\mathbf{v}_1 , smaller eigenvalue) and robustness (\mathbf{v}_2 , greater eigenvalue) (Fig. 1E, arrows)
170 agree with error contours (Fig. 1E contours) and have diminished or preserved hub frequency, re-

171 spectsively (Fig. 1F activity traces). The directionality of \mathbf{v}_2 suggests that changes in conductance
 172 along this parameter combination will most preserve hub neuron firing between the intrinsic rates
 173 of the pyloric and gastric mill rhythms. Importantly and unlike alternative techniques, once an
 174 EPI distribution has been learned, the modes and Hessians of the distribution can be measured
 175 with trivial computation (see Section 5.1.2).

176 In the following sections, we demonstrate EPI on three neural circuit models across ranges of
 177 biological realism, neural system function, and network scale. First, we demonstrate the superior
 178 scalability of EPI compared to alternative techniques by inferring high-dimensional distributions
 179 of recurrent neural network connectivities that exhibit amplified, yet stable responses. Next, in a
 180 model of primary visual cortex [46,47], we show how EPI discovers parametric degeneracy, revealing
 181 how input variability across neuron types affects the excitatory population. Finally, in a model of
 182 superior colliculus [48], we used EPI to capture multiple parametric regimes of task switching, and
 183 queried the dimensions of parameter sensitivity to characterize each regime.

184 **3.3 Scaling inference of recurrent neural network connectivity with EPI**

185 To understand how EPI scales in comparison to existing techniques, we consider recurrent neu-
 186 ral networks (RNNs). Transient amplification is a hallmark of neural activity throughout cortex,
 187 and is often thought to be intrinsically generated by recurrent connectivity in the responding cor-
 188 tical area [43–45]. It has been shown that to generate such amplified, yet stabilized responses,
 189 the connectivity of RNNs must be non-normal [43, 50], and satisfy additional constraints [51]. In
 190 theoretical neuroscience, RNNs are optimized and then examined to show how dynamical systems
 191 could execute a given computation [52, 53], but such biologically realistic constraints on connec-
 192 tivity [43, 50, 51] are ignored for simplicity or because constrained optimization is difficult. In
 193 general, access to distributions of connectivity that produce theoretical criteria like stable amplifi-
 194 cation, chaotic fluctuations [10], or low tangling [54] would add scientific value to existing research
 195 with RNNs. Here, we use EPI to learn RNN connectivities producing stable amplification, and
 196 demonstrate the superior scalability and efficiency of EPI to alternative approaches.

197 We consider a rank-2 RNN with N neurons having connectivity $W = UV^\top$ and dynamics

$$\tau \dot{\mathbf{x}} = -\mathbf{x} + W\mathbf{x}, \quad (4)$$

198 where $U = [\mathbf{U}_1 \ \mathbf{U}_2] + g\chi^{(U)}$, $V = [\mathbf{V}_1 \ \mathbf{V}_2] + g\chi^{(V)}$, $\mathbf{U}_1, \mathbf{U}_2, \mathbf{V}_1, \mathbf{V}_2 \in [-1, 1]^N$, and $\chi_{i,j}^{(U)}, \chi_{i,j}^{(V)} \sim$
 199 $\mathcal{N}(0, 1)$. We infer connectivity parameters $\mathbf{z} = [\mathbf{U}_1, \mathbf{U}_2, \mathbf{V}_1, \mathbf{V}_2]$ that produce stable amplification.

200 Two conditions are necessary and sufficient for RNNs to exhibit stable amplification [51]: $\text{real}(\lambda_1) <$
 201 1 and $\lambda_1^s > 1$, where λ_1 is the eigenvalue of W with greatest real part and λ^s is the maximum
 202 eigenvalue of $W^s = \frac{W+W^\top}{2}$. RNNs with $\text{real}(\lambda_1) = 0.5 \pm 0.5$ and $\lambda_1^s = 1.5 \pm 0.5$ will be stable with
 203 modest decay rate ($\text{real}(\lambda_1)$ close to its upper bound of 1) and exhibit modest amplification (λ_1^s
 204 close to its lower bound of 1). EPI can naturally condition on this emergent property

$$\begin{aligned}\mathcal{X} : \mathbb{E}_{\mathbf{z}, \mathbf{x}} \begin{bmatrix} \text{real}(\lambda_1) \\ \lambda_1^s \end{bmatrix} &= \begin{bmatrix} 0.5 \\ 1.5 \end{bmatrix} \\ \text{Var}_{\mathbf{z}, \mathbf{x}} \begin{bmatrix} \text{real}(\lambda_1) \\ \lambda_1^s \end{bmatrix} &= \begin{bmatrix} 0.25^2 \\ 0.25^2 \end{bmatrix}.\end{aligned}\quad (5)$$

205 Variance constraints predicate that the majority of the distribution (within two standard devia-
 206 tions) are within the specified ranges.

207 For comparison, we infer the parameters \mathbf{z} likely to produce stable amplification using two al-
 208 ternative simulation-based inference approaches. Sequential Monte Carlo approximate bayesian
 209 computation (SMC-ABC) [26] is a rejection sampling approach that uses SMC techniques to im-
 210 prove efficiency, and sequential neural posterior estimation (SNPE) [35] approximates posteriors
 211 with deep probability distributions (see Section 5.1.1). Unlike EPI, these statistical inference tech-
 212 niques do not constrain the predictions of the inferred distribution, so they were run by conditioning
 213 on an exemplar dataset $\mathbf{x}_0 = \boldsymbol{\mu}$, following standard practice with these methods [26, 35]. To com-
 214 pare the efficiency of these different techniques, we measured the time and number of simulations
 215 necessary for the distance of the predictive mean to be less than 0.5 from $\boldsymbol{\mu} = \mathbf{x}_0$ (see Section 5.3).

216 As the number of neurons N in the RNN, and thus the dimension of the parameter space $\mathbf{z} \in$
 217 $[-1, 1]^{4N}$, is scaled, we see that EPI converges at greater speed and at greater dimension than
 218 SMC-ABC and SNPE (Fig. 2A). It also becomes most efficient to use EPI in terms of simulation
 219 count at $N = 50$ (Fig. 2B). It is well known that ABC techniques struggle in parameter spaces
 220 of modest dimension [55], yet we were careful to assess the scalability of SNPE, which is a more
 221 closely related methodology to EPI. Between EPI and SNPE, we closely controlled the number of
 222 parameters in deep probability distributions by dimensionality (Fig. S5), and tested more aggressive
 223 SNPE hyperparameter choices when SNPE failed to converge (Fig. S6). In this analysis, we see that
 224 deep inference techniques EPI and SNPE are far more amenable to inference of high dimensional
 225 RNN connectivities than rejection sampling techniques like SMC-ABC, and that EPI outperforms
 226 SNPE in both wall time (elapsed real time) and simulation count.

227 No matter the number of neurons, EPI always produces connectivity distributions with mean and

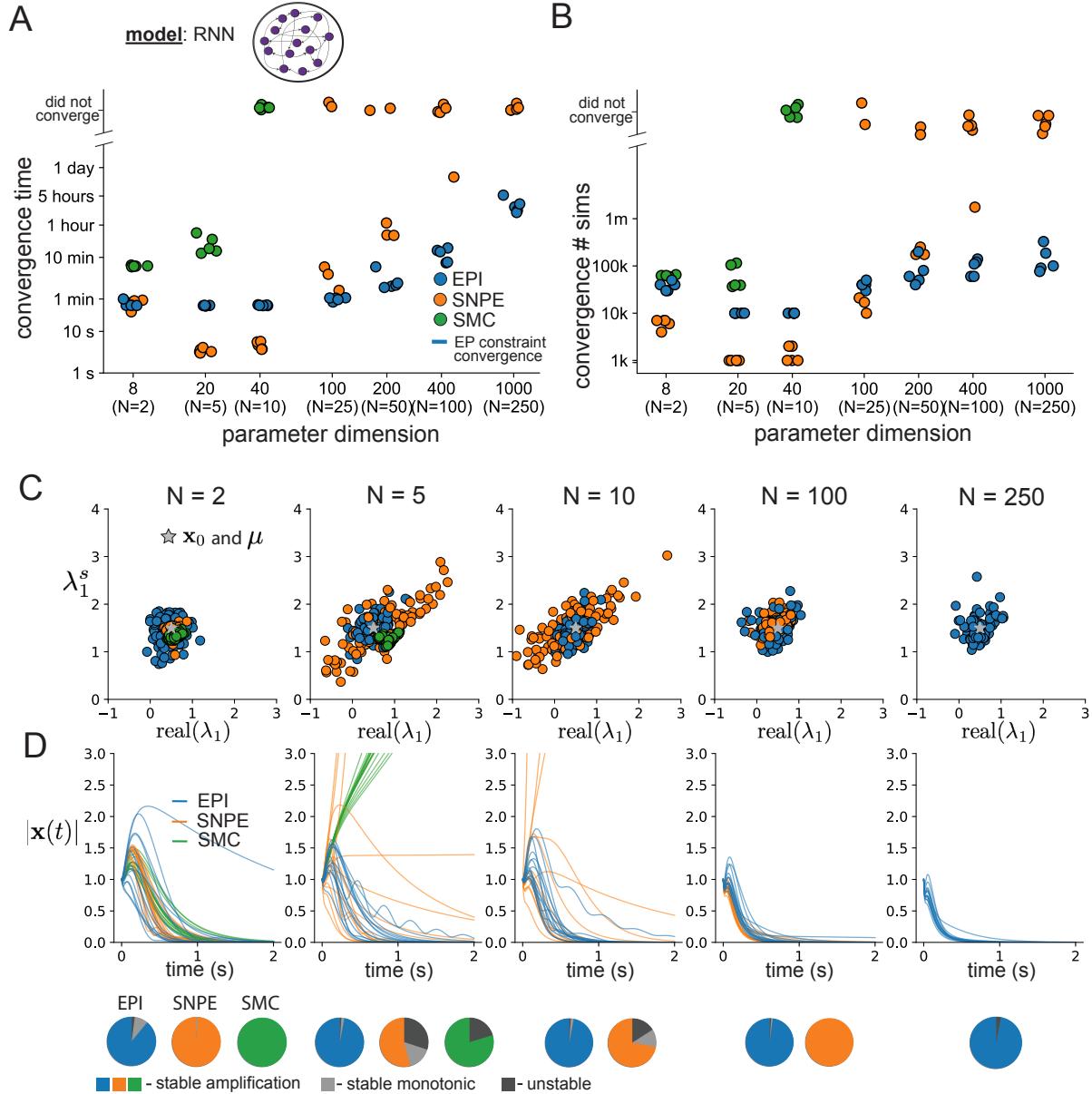


Figure 2: **A.** Wall time of EPI (blue), SNPE (orange), and SMC-ABC (green) to converge on RNN connectivities producing stable amplification. Each dot shows convergence time for an individual random seed. For reference, the mean wall time for EPI to achieve its full constraint convergence (means and variances) is shown (blue line). **B.** Simulation count of each algorithm to achieve convergence. Same conventions as A. **C.** The predictive distributions of connectivities inferred by EPI (blue), SNPE (orange), and SMC-ABC (green), with reference to $\mathbf{x}_0 = \boldsymbol{\mu}$ (gray star). **D.** Simulations of networks inferred by each method ($\tau = 100ms$). Each trace (15 per algorithm) corresponds to simulation of one z . (Below) Ratio of obtained samples producing stable amplification, stable monotonic decay, and instability.

228 variance of $\text{real}(\lambda_1)$ and λ_1^s according to \mathcal{X} (Fig. 2C, blue). For the dimensionalities in which
229 SMC-ABC is tractable, the inferred parameters are concentrated and offset from the exemplar
230 dataset \mathbf{x}_0 (Fig. 2C, green). When using SNPE, the predictions of the inferred parameters are
231 highly concentrated at some RNN sizes and widely varied in others (Fig. 2C, orange). We see these
232 properties reflected in simulations from the inferred distributions: EPI produces a consistent variety
233 of stable, amplified activity norms $|\mathbf{x}(t)|$, SMC-ABC produces a limited variety of responses, and the
234 changing variety of responses from SNPE emphasizes the control of EPI on parameter predictions
235 (Fig. 2D). Even for moderate neuron counts, the predictions of the inferred distribution of SNPE
236 are highly dependent on N and g , while EPI maintains the emergent property across choices of
237 RNN (see Section 5.3.5).

238 To understand these differences, note that EPI outperforms SNPE in high dimensions by using
239 gradient information (from $\nabla_{\mathbf{z}}[\text{real}(\lambda_1), \lambda_1^s]^\top$). This choice agrees with recent speculation that such
240 gradient information could improve the efficiency of simulation-based inference techniques [56],
241 as well as reflecting the classic tradeoff between gradient-based and sampling-based estimators
242 (scaling and speed versus generality). Since gradients of the emergent property are necessary
243 in EPI optimization, gradient tractability is a key criteria when determining the suitability of a
244 simulation-based inference technique. If the emergent property gradient is efficiently calculated,
245 EPI is a clear choice for inferring high dimensional parameter distributions. In the next two sections,
246 we use EPI for novel scientific insight by examining the structure of inferred distributions.

247 **3.4 EPI reveals how recurrence with multiple inhibitory subtypes governs ex-**
248 **citatory variability in a V1 model**

249 Dynamical models of excitatory (E) and inhibitory (I) populations with supralinear input-output
250 function have succeeded in explaining a host of experimentally documented phenomena in primary
251 visual cortex (V1). In a regime characterized by inhibitory stabilization of strong recurrent excita-
252 tion, these models give rise to paradoxical responses [12], selective amplification [43, 50], surround
253 suppression [57] and normalization [58]. Recent theoretical work [59] shows that stabilized E-I
254 models reproduce the effect of variability suppression [60]. Furthermore, experimental evidence
255 shows that inhibition is composed of distinct elements – parvalbumin (P), somatostatin (S), VIP
256 (V) – composing 80% of GABAergic interneurons in V1 [61–63], and that these inhibitory cell
257 types follow specific connectivity patterns (Fig. 3A) [64]. Here, we use EPI on a model of V1 with
258 biologically realistic connectivity to show how the structure of input across neuron types affects

259 the variability of the excitatory population – the population largely responsible for projecting to
 260 other brain areas [65].

261 We considered response variability of a nonlinear dynamical V1 circuit model (Fig. 3A) with a state
 262 comprised of each neuron-type population’s rate $\mathbf{x} = [x_E, x_P, x_S, x_V]^\top$. Each population receives
 263 recurrent input $W\mathbf{x}$, where W is the effective connectivity matrix (see Section 5.4) and an external
 264 input with mean \mathbf{h} , which determines population rate via supralinear nonlinearity $\phi(\cdot) = [\cdot]_+^2$. The
 265 external input has an additive noisy component ϵ with variance $\sigma^2 = [\sigma_E^2, \sigma_P^2, \sigma_S^2, \sigma_V^2]$. This noise
 266 has a slower dynamical timescale $\tau_{\text{noise}} > \tau$ than the population rate, allowing fluctuations around
 267 a stimulus-dependent steady-state (Fig. 3B). This model is the stochastic stabilized supralinear
 268 network (SSSN) [59]

$$\tau \frac{d\mathbf{x}}{dt} = -\mathbf{x} + \phi(W\mathbf{x} + \mathbf{h} + \epsilon), \quad (6)$$

269 generalized to have multiple inhibitory neuron types. It introduces stochasticity to four neuron-
 270 type models of V1 [46]. Stochasticity and inhibitory multiplicity introduce substantial complexity
 271 to the mathematical treatment of this problem (see Section 5.4.5) motivating the analysis of this
 272 model with EPI. Here, we consider fixed weights W and input \mathbf{h} [47], and study the effect of input
 273 variability $\mathbf{z} = [\sigma_E, \sigma_P, \sigma_S, \sigma_V]^\top$ on excitatory variability.

274 We quantify levels of E-population variability by studying two emergent properties

$$\begin{aligned} \mathcal{X}(5\text{Hz}) : \mathbb{E}_{\mathbf{z}, \mathbf{x}} [s_E(\mathbf{x}; \mathbf{z})] &= 5\text{Hz} & \mathcal{X}(10\text{Hz}) : \mathbb{E}_{\mathbf{z}, \mathbf{x}} [s_E(\mathbf{x}; \mathbf{z})] &= 10\text{Hz} \\ \text{Var}_{\mathbf{z}, \mathbf{x}} [s_E(\mathbf{x}; \mathbf{z})] &= 1\text{Hz}^2 & \text{Var}_{\mathbf{z}, \mathbf{x}} [s_E(\mathbf{x}; \mathbf{z})] &= 1\text{Hz}^2, \end{aligned} \quad (7)$$

275 where $s_E(\mathbf{x}; \mathbf{z})$ is the standard deviation of the stochastic E -population response about its steady
 276 state (Fig. 3C). In the following analyses, we select 1Hz^2 variance such that the two emergent
 277 properties do not overlap in $s_E(\mathbf{z}; \mathbf{x})$.

278 First, we ran EPI to obtain parameter distribution $q_\theta(\mathbf{z} \mid \mathcal{X}(5\text{Hz}))$ producing E-population vari-
 279 ability around 5Hz (Fig. 3D). From the marginal distribution of σ_E and σ_P (Fig. 3D, top-left),
 280 we can see that $s_E(\mathbf{x}; \mathbf{z})$ is sensitive to various combinations of σ_E and σ_P . Alternatively, both σ_S
 281 and σ_V are degenerate with respect to $s_E(\mathbf{x}; \mathbf{z})$ evidenced by the unexpectedly high variability in
 282 those dimensions (Fig. 3D, bottom-right). Together, these observations imply a curved path with
 283 respect to $s_E(\mathbf{x}; \mathbf{z})$ of 5Hz, which is indicated by the modes along σ_P (Fig. 3E).

284 Figure 3E suggests a quadratic relationship in E-population fluctuations and the standard deviation
 285 of E- and P-population input; as the square of either σ_E or σ_P increases, the other compensates by
 286 decreasing to preserve the level of $s_E(\mathbf{x}; \mathbf{z})$. This quadratic relationship is preserved at greater level

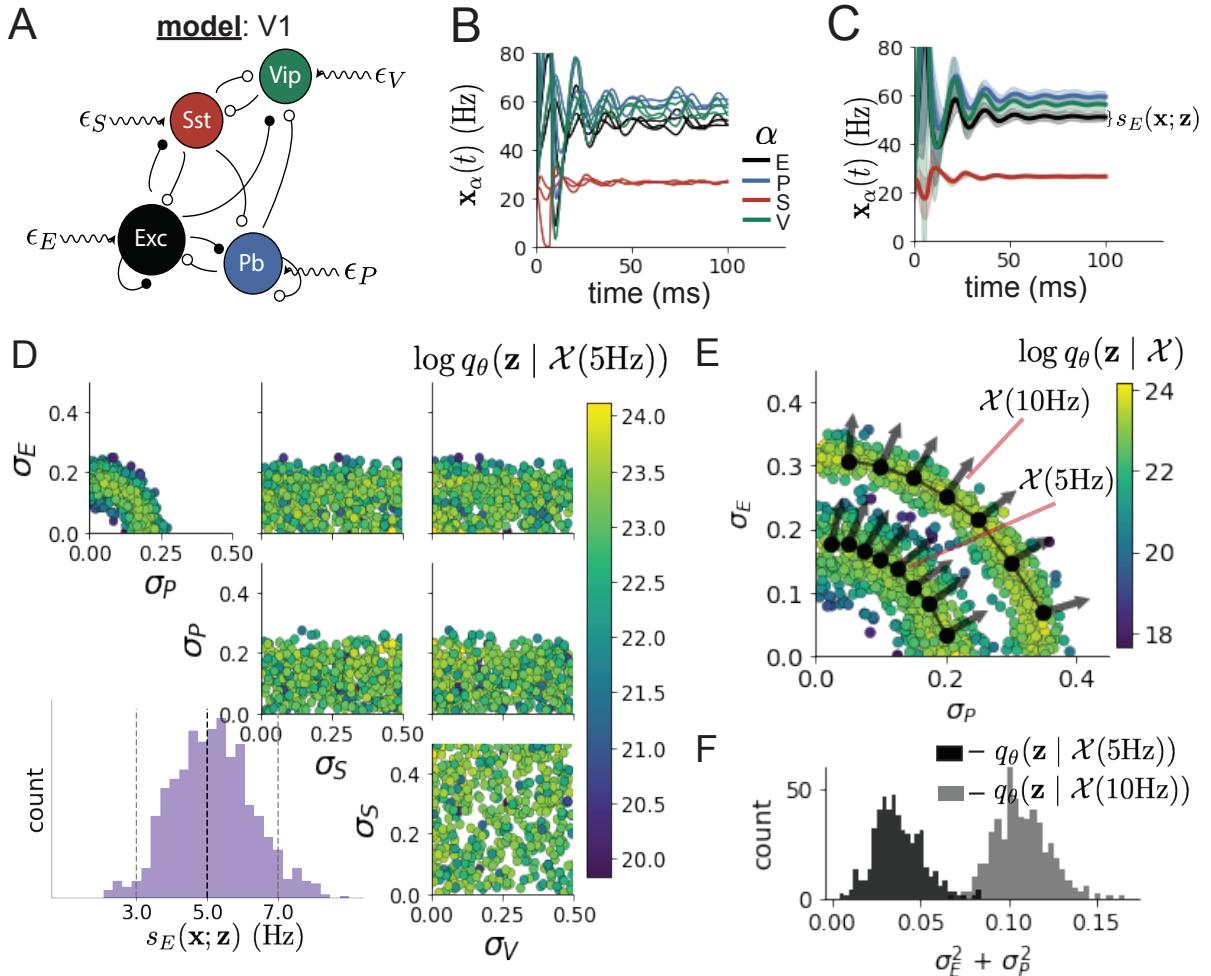


Figure 3: Emergent property inference in the stochastic stabilized supralinear network (SSSN)

A. Four-population model of primary visual cortex with excitatory (black), parvalbumin (blue), somatostatin (red), and VIP (green) neurons (excitatory and inhibitory projections filled and unfilled, respectively). Some neuron-types largely do not form synaptic projections to others ($|W_{\alpha_1, \alpha_2}| < 0.025$). Each neural population receives a baseline input \mathbf{h}_b , and the E- and P- populations also receive a contrast-dependent input \mathbf{h}_c . Additionally, each neural population receives a slow noisy input ϵ .

B. Transient network responses of the SSSN model. Traces are independent trials with varying initialization $\mathbf{x}(0)$ and noise ϵ .

C. Mean (solid line) and standard deviation $s_E(\mathbf{x}; \mathbf{z})$ (shading) across 100 trials.

D. EPI distribution of noise parameters \mathbf{z} conditioned on E-population variability. The EPI predictive distribution of $s_E(\mathbf{x}; \mathbf{z})$ is show on the bottom-left.

E. (Top) Enlarged visualization of the σ_E - σ_P marginal distribution of EPI $q_\theta(\mathbf{z} | \mathcal{X}(5\text{Hz}))$ and $q_\theta(\mathbf{z} | \mathcal{X}(10\text{Hz}))$. Each black dot shows the mode at each σ_P . The arrows show the most sensitive dimensions of the Hessian evaluated at these modes.

F. The predictive distributions of $\sigma_E^2 + \sigma_P^2$ of each inferred distribution $q_\theta(\mathbf{z} | \mathcal{X}(5\text{Hz}))$ and $q_\theta(\mathbf{z} | \mathcal{X}(10\text{Hz}))$.

287 of E-population variability $\mathcal{X}(10\text{Hz})$ (Fig. 3E and S8). Indeed, the sum of squares of σ_E and σ_P is
288 larger in $q_{\theta}(\mathbf{z} \mid \mathcal{X}(10\text{Hz}))$ than $q_{\theta}(\mathbf{z} \mid \mathcal{X}(5\text{Hz}))$ (Fig 3F, $p < 1 \times 10^{-10}$), while the sum of squares of
289 σ_S and σ_V are not significantly different in the two EPI distributions (Fig. S10, $p = .40$), in which
290 parameters were bounded from 0 to 0.5. The strong interaction between E- and P-population input
291 variability on excitatory variability is intriguing, since this circuit exhibits a paradoxical effect in
292 the P-population (and no other inhibitory types) (Fig. S11), meaning that the E-population is
293 P-stabilized. Future research may uncover a link between the population of network stabilization
294 and compensatory interactions governing excitatory variability.

295 EPI revealed the quadratic dependence of excitatory variability on input variability to the E- and
296 P-populations, as well as its independence to input from the other two inhibitory populations.
297 In a simplified model ($\tau = \tau_{\text{noise}}$), it can be shown that surfaces of equal variance are ellipsoids
298 as a function of σ (see Section 5.4.5). Nevertheless, the sensitive and degenerate parameters are
299 intractable to predict mathematically, since the covariance matrix depends on the steady-state
300 solution of the network [59, 66], and terms in the covariance expression increase quadratically with
301 each additional neuron-type population (see also Section 5.4.5). By pointing out this mathematical
302 complexity, we emphasize the value of EPI for gaining understanding about theoretical models
303 when mathematical analysis becomes onerous or impractical.

304 3.5 EPI identifies two regimes of rapid task switching

305 It has been shown that rats can learn to switch from one behavioral task to the next on randomly
306 interleaved trials [67], and an important question is what neural mechanisms produce this compu-
307 tation. In this experimental setup, rats were given an explicit task cue on each trial, either Pro
308 or Anti. After a delay period, rats were shown a stimulus, and made a context (task) dependent
309 response (Fig. 4A). In the Pro task, rats were required to orient towards the stimulus, while in
310 the Anti task, rats were required to orient away from the stimulus. Pharmacological inactivation
311 of the SC impaired rat performance, and time-specific optogenetic inactivation revealed a crucial
312 role for the SC on the cognitively demanding Anti trials [48]. These results motivated a nonlinear
313 dynamical model of the SC containing four functionally-defined neuron-type populations. In Duan
314 et al. 2019, a computationally intensive procedure was used to obtain a set of 373 connectivity
315 parameters that qualitatively reproduced these optogenetic inactivation results. To build upon
316 the insights of this previous work, we use the probabilistic tools afforded by EPI to identify and
317 characterize two linked, yet distinct regimes of rapid task switching connectivity.

318 In this SC model, there are Pro- and Anti-populations in each hemisphere (left (L) and right (R))
 319 with activity variables $\mathbf{x} = [x_{LP}, x_{LA}, x_{RP}, x_{RA}]^\top$ [48]. The connectivity of these populations is
 320 parameterized by self sW , vertical vW , diagonal dW and horizontal hW connections (Fig. 4B). The
 321 input \mathbf{h} is comprised of a positive cue-dependent signal to the Pro or Anti populations, a positive
 322 stimulus-dependent input to either the Left or Right populations, and a choice-period input to the
 323 entire network (see Section 5.5.1). Model responses are bounded from 0 to 1 as a function ϕ of an
 324 internal variable \mathbf{u}

$$\begin{aligned} \tau \frac{d\mathbf{u}}{dt} &= -\mathbf{u} + W\mathbf{x} + \mathbf{h} + d\mathbf{B} \\ \mathbf{x} &= \phi(\mathbf{u}). \end{aligned} \quad (8)$$

325 The model responds to the side with greater Pro neuron activation; e.g. the response is left if
 326 $x_{LP} > x_{RP}$ at the end of the trial. Here, we use EPI to determine the network connectivity
 327 $\mathbf{z} = [sW, vW, dW, hW]^\top$ that produces rapid task switching.
 328 Rapid task switching is formalized mathematically as an emergent property with two statistics:
 329 accuracy in the Pro task $p_P(\mathbf{x}; \mathbf{z})$ and Anti task $p_A(\mathbf{x}; \mathbf{z})$. We stipulate that accuracy be on average
 330 .75 in each task with variance .075²

$$\begin{aligned} \mathcal{X} : \mathbb{E}_{\mathbf{z}} \begin{bmatrix} p_P(\mathbf{x}; \mathbf{z}) \\ p_A(\mathbf{x}; \mathbf{z}) \end{bmatrix} &= \begin{bmatrix} .75 \\ .75 \end{bmatrix} \\ \text{Var}_{\mathbf{z}} \begin{bmatrix} p_P(\mathbf{x}; \mathbf{z}) \\ p_A(\mathbf{x}; \mathbf{z}) \end{bmatrix} &= \begin{bmatrix} .075^2 \\ .075^2 \end{bmatrix}. \end{aligned} \quad (9)$$

331 75% accuracy is a realistic level of performance in each task, and with the chosen variance, inferred
 332 models will not exhibit fully random responses (50%), nor perfect performance (100%).
 333 The EPI inferred distribution (Fig. 4C) produces Pro and Anti task accuracies (Fig. 4C, bottom-left)
 334 consistent with rapid task switching (Equation 9). This parameter distribution has rich structure
 335 that is not captured well by simple linear correlations (Fig. S12). Specifically, the shape
 336 of the EPI distribution is sharply bent, matching ground truth structure indicated by brute-force
 337 sampling (Fig. S18). This is most saliently observed in the marginal distribution of $sW-hW$ (Fig.
 338 4C top-right), where anticorrelation between sW and hW switches to correlation with decreasing
 339 sW . By identifying the modes of the EPI distribution $\mathbf{z}^*(sW)$ at different values of sW (Fig. 4C
 340 red/purple dots), we can quantify this change in distributional structure with the sensitivity dimension
 341 $\mathbf{v}_1(\mathbf{z})$ (Fig. 4C red/purple arrows). Note that the directionality of these sensitivity dimensions
 342 at $\mathbf{z}^*(sW)$ changes distinctly with sW , and are perpendicular to the robust dimensions of the EPI

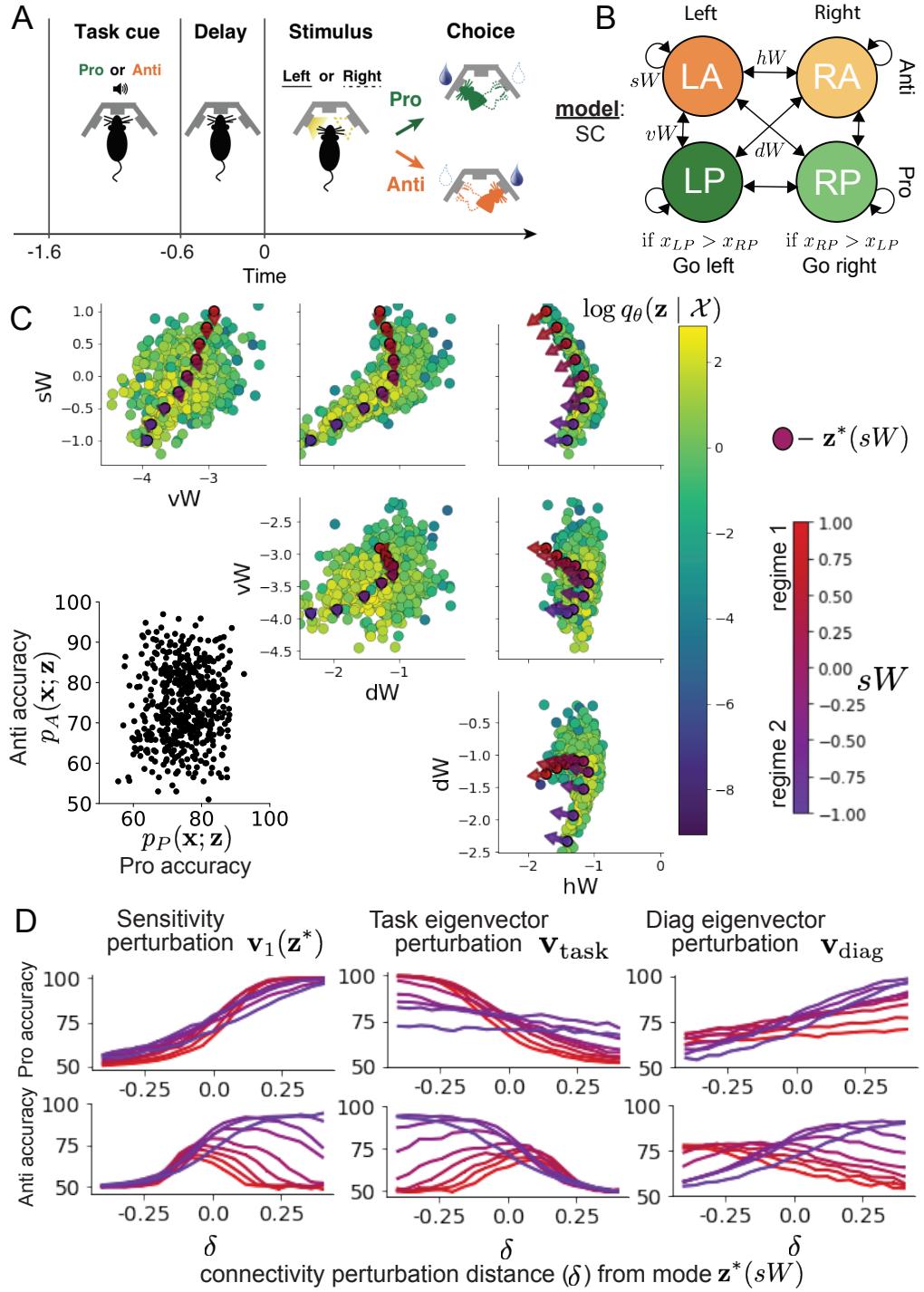


Figure 4: **A.** Rapid task switching behavioral paradigm (see text). **B.** Model of superior colliculus (SC). Neurons: LP - Left Pro, RP - Right Pro, LA - Left Anti, RA - Right Anti. Parameters: sW - self, hW - horizontal, vW - vertical, dW - diagonal weights. **C.** The EPI inferred distribution of rapid task switching networks. Red/purple parameters indicate modes $\mathbf{z}^*(sW)$ colored by sW . Sensitivity vectors $\mathbf{v}_1(\mathbf{z}^*)$ are shown by arrows. (Bottom-left) EPI predictive distribution of task accuracies. **D.** Mean and standard error ($N_{\text{test}} = 25$, bars not visible) of accuracy in Pro (top) and Anti (bottom) tasks after perturbing connectivity away from mode along $\mathbf{v}_1(\mathbf{z}^*)$ (left), \mathbf{v}_{task} (middle), and \mathbf{v}_{diag} (right).

343 distribution that preserve rapid task switching. These two directionalities of sensitivity motivate
344 the distinction of connectivity into two regimes, which produce different types of responses in the
345 Pro and Anti tasks (Fig. S13).

346 When perturbing connectivity along the sensitivity dimension away from the modes

$$\mathbf{z} = \mathbf{z}^*(sW) + \delta\mathbf{v}_1(\mathbf{z}^*(sW)), \quad (10)$$

347 Pro accuracy monotonically increases in both regimes (Fig. 4D, top-left). However, there is a stark
348 difference between regimes in Anti accuracy. Anti accuracy falls in either direction of \mathbf{v}_1 in regime 1,
349 yet monotonically increases along with Pro accuracy in regime 2 (Fig. 4D, bottom-left). The sharp
350 change in local structure of the EPI distribution is therefore explained by distinct sensitivities:
351 Anti accuracy diminishes in only one or both directions of the sensitivity perturbation.

352 To understand the mechanisms differentiating the two regimes, we can make connectivity pertur-
353 bations along dimensions that only modify a single eigenvalue of the connectivity matrix. These
354 eigenvalues λ_{all} , λ_{side} , λ_{task} , and λ_{diag} correspond to connectivity eigenmodes with intuitive roles
355 in processing in this task (Fig. S14A). For example, greater λ_{task} will strengthen internal repre-
356 sentations of task, while greater λ_{diag} will amplify dominance of Pro and Anti pairs in opposite
357 hemispheres (Section 5.5.7). Unlike the sensitivity dimension, the dimensions \mathbf{v}_a that perturb
358 isolated connectivity eigenvalues λ_a for $a \in \{\text{all}, \text{side}, \text{task}, \text{diag}\}$ are independent of $\mathbf{z}^*(sW)$ (see
359 Section 5.5.7), e.g.

$$\mathbf{z} = \mathbf{z}^*(sW) + \delta\mathbf{v}_{\text{task}}. \quad (11)$$

360 Connectivity perturbation analyses reveal that decreasing λ_{task} has a very similar effect on Anti
361 accuracy as perturbations along the sensitivity dimension (Fig. 4D, middle). The similar effects
362 of perturbations along the sensitivity dimension $\mathbf{v}_1(\mathbf{z}^*)$ and reduction of task eigenvalue (via per-
363 turbations along $-\mathbf{v}_{\text{task}}$) suggest that there is a carefully tuned strength of task representation in
364 connectivity regime 1, which if disturbed results in random Anti trial responses. Finally, we rec-
365 ognize that increasing λ_{diag} has opposite effects on Anti accuracy in each regime (Fig. 4D, right).
366 In the next section, we build on these mechanistic characterizations of each regime by examining
367 their resilience to optogenetic inactivation.

368 **3.6 EPI inferred SC connectivities reproduce results from optogenetic inacti-**
369 **vation experiments**

370 During the delay period of this task, the circuit must prepare to execute the correct task according
371 to the presented cue. The circuit must then maintain a representation of task throughout the delay
372 period, which is important for correct execution of the Anti task. Duan et al. found that bilateral
373 optogenetic inactivation of SC during the delay period consistently decreased performance in the
374 Anti task, but had no effect on the Pro task (Fig. 5A) [48]. The distribution of connectivities
375 inferred by EPI exhibited this same effect in simulation at high optogenetic strengths γ , which
376 reduce the network activities $\mathbf{x}(t)$ by a factor $1 - \gamma$ (Fig. 5B) (see Section 5.5.8).

377 To examine how connectivity affects response to delay period inactivation, we grouped connectivi-
378 ties of the EPI distribution along the continuum linking regimes 1 and 2 of Section 3.5. $Z(sW)$ is
379 the set of EPI samples for which the closest mode was $\mathbf{z}^*(sW)$ (see Section 5.5.4). In the following
380 analyses, we examine how error, and the influence of connectivity eigenvalue on Anti error change
381 along this continuum of connectivities. Obtaining the parameter samples for these analysis with
382 the learned EPI distribution was more than 20,000 times faster than a brute force approach (see
383 Section 5.5.5).

384 The mean increase in Anti error of the EPI distribution is closest to the experimentally measured
385 value of 7% at $\gamma = 0.675$ (Fig. 5B, black dot). At this level of optogenetic strength, regime
386 1 exhibits an increase in Anti error with delay period silencing (Fig. 5C, left), while regime 2
387 does not. In regime 1, greater λ_{task} and λ_{diag} decrease Anti error (Fig. 5C, right). In other words,
388 stronger task representations and diagonal amplification make the SC model more resilient to delay
389 period silencing in the Anti task. This complements the finding from Duan et al. 2019 [48] that
390 λ_{task} and λ_{diag} improve Anti accuracy.

391 At roughly $\gamma = 0.85$ (Fig. 5B, gray dot), the Anti error saturates, while Pro error remains at
392 zero. Following delay period inactivation at this optogenetic strength, there are strong similarities
393 in the responses of Pro and Anti trials during the choice period (Fig. 5D, left). We interpreted
394 these similarities to suggest that delay period inactivation at this saturated level flips the internal
395 representation of task (from Anti to Pro) in the circuit model. A flipped task representation
396 would explain why the Anti error saturates at 50%: the average Anti accuracy in EPI inferred
397 connectivities is 75%, but is 25% when the internal representation is flipped during delay period
398 silencing. This hypothesis prescribes a model of Anti accuracy during delay period silencing of

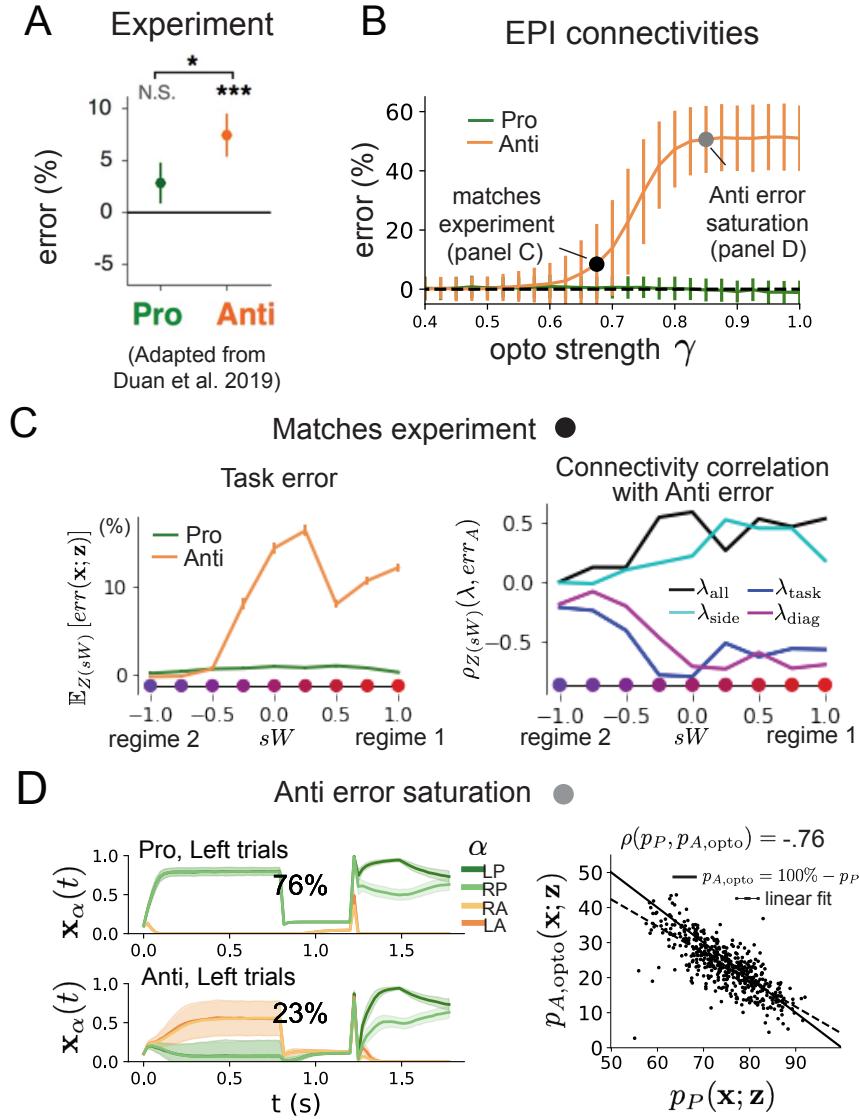


Figure 5: **A.** Mean and standard error (bars) across recording sessions of task error following delay period optogenetic inactivation in rats. **B.** Mean and standard deviation (bars) of task error induced by delay period inactivation of varying optogenetic strength γ across the EPI distribution. **C.** (Left) Mean and standard error of Pro and Anti error from regime 1 to regime 2 at $\gamma = 0.675$. (Right) Correlations of connectivity eigenvalues with Anti error from regime 1 to regime 2 at $\gamma = 0.675$. **D.** (Left) Mean and standard deviation (shading) of responses of the SC model at the mode of the EPI distribution to delay period inactivation at $\gamma = 0.85$. Accuracy in Pro (top) and Anti (bottom) task is shown as a percentage. (Right) Anti accuracy following delay period inactivation at $\gamma = 0.85$ versus accuracy in the Pro task across connectivities in the EPI distribution.

399 $p_{A,\text{opto}} = 100\% - p_P$, which is fit closely across both regimes of the EPI inferred connectivities (Fig.
400 5D, right). Similarities between Pro and Anti trial responses were not present at the experiment-
401 matching level of $\gamma = 0.675$ (Fig. S16 left) and neither was anticorrelation in p_P and $p_{A,\text{opto}}$ (Fig.
402 S16 right).

403 In summary, the connectivity inferred by EPI to perform rapid task switching replicated results
404 from optogenetic silencing experiments. We found that at levels of optogenetic strength matching
405 experimental levels of Anti error, only one regime actually exhibited the effect. This connectivity
406 regime is less resilient to optogenetic perturbation, and perhaps more biologically realistic. Finally,
407 we characterized the pathology in Anti error that occurs in both regimes when optogenetic strength
408 is increased to high levels, leading to a mechanistic hypothesis that is experimentally testable.
409 The probabilistic tools afforded by EPI yielded this insight: we identified two regimes and the
410 continuum of connectivities between them by taking gradients of parameter probabilities in the EPI
411 distribution, we identified sensitivity dimensions by measuring the Hessian of the EPI distribution,
412 and we obtained many parameter samples at each step along the continuum at an efficient rate.

413 4 Discussion

414 In neuroscience, machine learning has primarily been used to reveal structure in neural datasets [20].
415 Careful inference procedures are developed for these statistical models allowing precise, quantitative
416 reasoning, which clarifies the way data informs beliefs about the model parameters. However, these
417 statistical models often lack resemblance to the underlying biology, making it unclear how to go
418 from the structure revealed by these methods, to the neural mechanisms giving rise to it. In
419 contrast, theoretical neuroscience has primarily focused on careful models of neural circuits and
420 the production of emergent properties of computation, rather than measuring structure in neural
421 datasets. In this work, we improve upon parameter inference techniques in theoretical neuroscience
422 with emergent property inference, harnessing deep learning towards parameter inference in neural
423 circuit models (see Section 5.1.1).

424 Methodology for statistical inference in circuit models has evolved considerably in recent years.
425 Early work used rejection sampling techniques [24–26], but EPI and another recently developed
426 methodology [35] employ deep learning to improve efficiency and provide flexible approximations.
427 SNPE has been used for posterior inference of parameters in circuit models conditioned upon
428 exemplar data used to represent computation, but it does not infer parameter distributions that

429 only produce the computation of interest like EPI (see Section 3.3). When strict control over the
430 predictions of the inferred parameters is necessary, EPI uses a constrained optimization technique
431 [38] (see Section 5.1.4) to make inference conditioned on the emergent property possible.

432 A key difference between EPI and SNPE, is that EPI uses gradients of the emergent property
433 throughout optimization. In Section 3.3, we showed that such gradients confer beneficial scaling
434 properties, but a concern remains that emergent property gradients may be too computationally
435 intensive. Even in a case of close biophysical realism with an expensive emergent property gradient,
436 EPI was run successfully on intermediate hub frequency in a 5-neuron subcircuit model of the
437 STG (Section 3.1). However, conditioning on the pyloric rhythm [68] in a model of the pyloric
438 subnetwork model [15] proved to be prohibitive with EPI. The pyloric subnetwork requires many
439 time steps for simulation and many key emergent property statistics (e.g. burst duration and
440 phase gap) are not calculable or easily approximated with differentiable functions. In such cases,
441 SNPE, which does not require differentiability of the emergent property, has proven useful [35].
442 In summary, choice of deep inference technique should consider emergent property complexity and
443 differentiability, dimensionality of parameter space, and the importance of constraining the model
444 behavior predicted by the inferred parameter distribution.

445 In this paper, we demonstrate the value of deep inference for parameter sensitivity analyses at
446 both the local and global level. With these techniques, flexible deep probability distributions are
447 optimized to capture global structure by approximating the full distribution of suitable parame-
448 ters. Importantly, the local structure of this deep probability distribution can be quantified at
449 any parameter choice, offering instant sensitivity measurements after fitting. For example, the
450 global structure captured by EPI revealed two distinct parameter regimes, which had different
451 local structure quantified by the deep probability distribution (see Section 5.5). In comparison,
452 bayesian MCMC is considered a popular approach for capturing global parameter structure [69],
453 but there is no variational approximation (the deep probability distribution in EPI), so sensitiv-
454 ity information is not queryable and sampling remains slow after convergence. Local sensitivity
455 analyses (e.g. [27]) may be performed independently at individual parameter samples, but these
456 methods alone do not capture the full picture in nonlinear, complex distributions. In contrast,
457 deep inference yields a probability distribution that produces a wholistic assessment of parameter
458 sensitivity at the local and global level, which we used in this study to make novel insights into
459 a range of theoretical models. Together, the abilities to condition upon emergent properties, the
460 efficient inference algorithm, and the capacity for parameter sensitivity analyses make EPI a useful

461 method for addressing inverse problems in theoretical neuroscience.

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471 **Data availability statement:**

472 The datasets generated during and/or analyzed during the current study are available from the
473 corresponding author upon reasonable request.

474 **Code availability statement:**

475 All software written for the current study is available at <https://github.com/cunningham-lab/epi>.

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719 **5 Methods**

720 **5.1 Emergent property inference (EPI)**

721 Solving inverse problems is an important part of theoretical neuroscience, since we must understand
722 how neural circuit models and their parameter choices produce computations. Recently, research on
723 machine learning methodology for neuroscience has focused on finding latent structure in large-scale
724 neural datasets, while research in theoretical neuroscience generally focuses on developing precise
725 neural circuit models that can produce computations of interest. By quantifying computation
726 into an *emergent property* through statistics of the emergent activity of neural circuit models, we
727 can adapt the modern technique of deep probabilistic inference towards solving inverse problems
728 in theoretical neuroscience. Here, we introduce a novel method for statistical inference, which
729 uses deep networks to learn parameter distributions constrained to produce emergent properties of
730 computation.

731 Consider model parameterization \mathbf{z} , which is a collection of scientifically meaningful variables that
732 govern the complex simulation of data \mathbf{x} . For example (see Section 3.1), \mathbf{z} may be the electrical
733 conductance parameters of an STG subcircuit, and \mathbf{x} the evolving membrane potentials of the five
734 neurons. In terms of statistical modeling, this circuit model has an intractable likelihood $p(\mathbf{x} | \mathbf{z})$,
735 which is predicated by the stochastic differential equations that define the model. From a theoretical
736 perspective, we are less concerned about the likelihood of an exemplar dataset \mathbf{x} , but rather the
737 emergent property of intermediate hub frequency (which implies a consistent dataset \mathbf{x}).

738 In this work, emergent properties \mathcal{X} are defined through the choice of emergent property statistic
739 $f(\mathbf{x}; \mathbf{z})$ (which is a vector of one or more statistics), and its means $\boldsymbol{\mu}$, and variances $\boldsymbol{\sigma}^2$:

$$\mathcal{X} : \mathbb{E}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] = \boldsymbol{\mu}, \quad \text{Var}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] = \boldsymbol{\sigma}^2. \quad (12)$$

740 In general, an emergent property may be a collection of first-, second-, or higher-order moments
741 of a group of statistics, but this study focuses on the case written in Equation 12. In the STG
742 example, intermediate hub frequency is defined by mean and variance constraints on the statistic
743 of hub neuron frequency $\omega_{\text{hub}}(\mathbf{x}; \mathbf{z})$ (Equations 2 and 3). Precisely, the emergent property statistics
744 $f(\mathbf{x}; \mathbf{z})$ must have means $\boldsymbol{\mu}$ and variances $\boldsymbol{\sigma}^2$ over the EPI distribution of parameters ($\mathbf{z} \sim q_{\boldsymbol{\theta}}(\mathbf{z})$) and
745 the data produced by those parameters ($\mathbf{x} \sim p(\mathbf{x} | \mathbf{z})$), where the inferred parameter distribution
746 $q_{\boldsymbol{\theta}}(\mathbf{z})$ itself is parameterized by deep network weights and biases $\boldsymbol{\theta}$.

747 In EPI, a deep probability distribution $q_{\boldsymbol{\theta}}(\mathbf{z})$ is optimized to approximate the parameter distribution

748 producing the emergent property \mathcal{X} . In contrast to simpler classes of distributions like the gaussian
 749 or mixture of gaussians, deep probability distributions are far more flexible and capable of fitting
 750 rich structure [36, 37]. In deep probability distributions, a simple random variable $\mathbf{z}_0 \sim q_0(\mathbf{z}_0)$ (we
 751 choose an isotropic gaussian) is mapped deterministically via a sequence of deep neural network
 752 layers ($g_1, \dots g_l$) parameterized by weights and biases $\boldsymbol{\theta}$ to the support of the distribution of interest:

$$\mathbf{z} = g_{\boldsymbol{\theta}}(\mathbf{z}_0) = g_l(\dots g_1(\mathbf{z}_0)) \sim q_{\boldsymbol{\theta}}(\mathbf{z}). \quad (13)$$

753 Such deep probability distributions embed the inferred distribution in a deep network. Once op-
 754 timized, this deep network representation of a distribution has remarkably useful properties: fast
 755 sampling and probability evaluations. Importantly, fast probability evaluations confer fast gradient
 756 and Hessian calculations as well.

757 Given this choice of circuit model and emergent property \mathcal{X} , $q_{\boldsymbol{\theta}}(\mathbf{z})$ is optimized via the neural
 758 network parameters $\boldsymbol{\theta}$ to find a maximally entropic distribution $q_{\boldsymbol{\theta}}^*$ within the deep variational
 759 family $\mathcal{Q} = \{q_{\boldsymbol{\theta}}(\mathbf{z}) : \boldsymbol{\theta} \in \Theta\}$ that produces the emergent property \mathcal{X} :

$$\begin{aligned} q_{\boldsymbol{\theta}}(\mathbf{z} | \mathcal{X}) &= q_{\boldsymbol{\theta}}^*(\mathbf{z}) = \operatorname{argmax}_{q_{\boldsymbol{\theta}} \in \mathcal{Q}} H(q_{\boldsymbol{\theta}}(\mathbf{z})) \\ \text{s.t. } \mathcal{X} &: \mathbb{E}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] = \boldsymbol{\mu}, \operatorname{Var}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] = \boldsymbol{\sigma}^2, \end{aligned} \quad (14)$$

760 where $H(q_{\boldsymbol{\theta}}(\mathbf{z})) = \mathbb{E}_{\mathbf{z}} [-\log q_{\boldsymbol{\theta}}(\mathbf{z})]$ is entropy. By maximizing the entropy of the inferred distribution
 761 $q_{\boldsymbol{\theta}}$, we select the most random distribution in family \mathcal{Q} that satisfies the constraints of the emergent
 762 property. Since entropy is maximized in Equation 14, EPI is equivalent to bayesian variational
 763 inference (see Section 5.1.6), which is why we specify the inferred distribution of EPI as conditioned
 764 upon emergent property \mathcal{X} with the notation $q_{\boldsymbol{\theta}}(\mathbf{z} | \mathcal{X})$. To run this constrained optimization, we
 765 use an augmented lagrangian objective, which is the standard approach for constrained optimization
 766 [70], and the approach taken to fit Maximum Entropy Flow Networks (MEFNs) [38]. This procedure
 767 is detailed in Section 5.1.4 and the pseudocode in Algorithm 1.

768 In the remainder of Section 5.1, we will explain the finer details and motivation of the EPI method.
 769 First, we explain related approaches and what EPI introduces to this domain (Section 5.1.1). Sec-
 770 ond, we describe the special class of deep probability distributions used in EPI called normalizing
 771 flows (Section 5.1.2). Then, we establish the known relationship between maximum entropy dis-
 772 tributions and exponential families (Section 5.1.3). Next, we explain the constrained optimization
 773 technique used to solve Equation 14 (Section 5.1.4). Then, we demonstrate the details of this opti-
 774 mization in a toy example (Section 5.1.5). Finally, we explain how EPI is equivalent to variational
 775 inference (Section 5.1.6).

776 **5.1.1 Related approaches**

777 When bayesian inference problems lack conjugacy, scientists use approximate inference methods like
778 variational inference (VI) [71] and Markov chain Monte Carlo (MCMC) [72,73]. After optimization,
779 variational methods return a parameterized posterior distribution, which we can analyze. Also, the
780 variational approximation is often chosen such that it permits fast sampling. In contrast MCMC
781 methods only produce samples from the approximated posterior distribution. No parameterized
782 distribution is estimated, and additional samples are always generated with the same sampling
783 complexity. Inference in models defined by systems of differential has been demonstrated with
784 MCMC [69], although this approach requires tractable likelihoods. Advancements have introduced
785 sampling [74], likelihood approximation [75], and uncertainty quantification techniques [76] to make
786 MCMC approaches more efficient and expand the class of applicable models.

787 Simulation-based inference [56] is model parameter inference in the absence of a tractable likeli-
788 hood function. The most prevalent approach to simulation-based inference is approximate bayesian
789 computation (ABC) [24], in which satisfactory parameter samples are kept from random prior sam-
790 pling according to a rejection heuristic. The obtained set of parameters do not have a probabilities,
791 and further insight about the model must be gained from examination of the parameter set and
792 their generated activity. Methodological advances to ABC methods have come through the use of
793 Markov chain Monte Carlo (MCMC-ABC) [25] and sequential Monte Carlo (SMC-ABC) [26] sam-
794 pling techniques. SMC-ABC is considered state-of-the-art ABC, yet this approach still struggles
795 to scale in dimensionality [55] (cf. Fig. 2). Still, this method has enjoyed much success in systems
796 biology [77]. Furthermore, once a parameter set has been obtained by SMC-ABC from a finite set
797 of particles, the SMC-ABC algorithm must be run again from scratch with a new population of
798 initialized particles to obtain additional samples.

799 For scientific model analysis, we seek a parameter distribution represented by an approximating
800 distribution as in variational inference [71]: a variational approximation that once optimized yields
801 fast analytic calculations and samples. For the reasons described above, ABC and MCMC tech-
802 niques are not suitable, since they only produce a set of parameter samples lacking probabilities
803 and have unchanging sampling rate. EPI infers parameters in circuit models using the MEFN [38]
804 algorithm with a deep variational approximation. The deep neural network of EPI (Fig. 1E) de-
805 fines the parametric form (with weights and biases as variational parameters θ) of the variational
806 approximation of the inferred parameter distribution $q_\theta(\mathbf{z} | \mathbf{x})$. The EPI optimization is enabled
807 using stochastic gradient techniques in the spirit of likelihood-free variational inference [34]. The

808 analytic relationship between EPI and variational inference is explained in Section 5.1.6.

809 We note that, during our preparation and early presentation of this work [78, 79], another work
810 has arisen with broadly similar goals: bringing statistical inference to mechanistic models of neural
811 circuits [35, 80, 81]. We are encouraged by this general problem being recognized by others in the
812 community, and we emphasize that these works offer complementary neuroscientific contributions
813 (different theoretical models of focus) and use different technical methodologies (ours is built on
814 our prior work [38], theirs similarly [82]).

815 The method EPI differs from SNPE in some key ways. SNPE belongs to a “sequential” class
816 of recently developed simulation-based inference methods in which two neural networks are used
817 for posterior inference. This first neural network is a deep probability distribution (normalizing
818 flow) used to estimate the posterior $p(\mathbf{z} | \mathbf{x})$ (SNPE) or the likelihood $p(\mathbf{x} | \mathbf{z})$ (sequential neural
819 likelihood (SNL) [83]). A recent approach uses an unconstrained neural network to estimate the
820 likelihood ratio (sequential neural ratio estimation (SNRE) [84]). In SNL and SNRE, MCMC
821 sampling techniques are used to obtain samples from the approximated posterior. This contrasts
822 with EPI and SNPE, which use deep probability distributions to model parameters, which facilitates
823 immediate measurements of sample probability, gradient, or Hessian for system analysis. The
824 second neural network in this sequential class of methods is the amortizer. This unconstrained
825 deep network maps data \mathbf{x} (or statistics $f(\mathbf{x}; \mathbf{z})$ or model parameters \mathbf{z}) to the weights and biases of
826 the first neural network. These methods are optimized on a conditional density (or ratio) estimation
827 objective. The data used to optimize this objective are generated via an adaptive procedure, in
828 which training data pairs $(\mathbf{x}_i, \mathbf{z}_i)$ become sequentially closer to the true data and posterior.

829 The approximating fidelity of the deep probability distribution in sequential approaches is opti-
830 mized to generalize across the training distribution of the conditioning variable. This generalization
831 property of the sequential methods can reduce the accuracy at the singular posterior of interest.
832 Whereas in EPI, the entire expressivity of the deep probability distribution is dedicated to learning
833 a single distribution as well as possible. The well-known inverse mapping problem of exponential
834 families [85] prohibits an amortization-based approach in EPI, since EPI learns an exponential fam-
835 ily distribution parameterized by its mean (in contrast to its natural parameter, see Section 5.1.3).
836 However, we have shown that the same two-network architecture of the sequential simulation-based
837 inference methods can be used for amortized inference in intractable exponential family posteriors
838 when using their natural parameterization [86].

839 Finally, one important differentiating factor between EPI and sequential simulation-based infer-

ence methods is that EPI leverages gradients $\nabla_{\mathbf{z}} f(\mathbf{x}; \mathbf{z})$ during optimization. These gradients can
 840 improve convergence time and scalability, as we have shown on an example conditioning low-rank
 841 RNN connectivity on the property of stable amplification (see Section 3.3). With EPI, we prove out
 842 the suggestion that a deep inference technique can improve efficiency by leveraging these emergent
 843 property gradients when they are tractable. Sequential simulation-based inference techniques may
 844 be better suited for scientific problems where $\nabla_{\mathbf{z}} f(\mathbf{x}; \mathbf{z})$ is intractable or unavailable, like when
 845 there is a nondifferentiable emergent property. However, the sequential simulation-based inference
 846 techniques cannot constrain the predictions of the inferred distribution in the manner of EPI.
 847

848 Structural identifiability analysis involves the measurement of sensitivity and unidentifiabilities in
 849 scientific models. Around a single parameter choice, one can measure the Jacobian. One approach
 850 for this calculation that scales well is EAR [28]. A popular efficient approach for systems of ODEs
 851 has been neural ODE adjoint [87] and its stochastic adaptation [88]. Casting identifiability as a
 852 statistical estimation problem, the profile likelihood works via iterated optimization while holding
 853 parameters fixed [27]. An exciting recent method is capable of recovering the functional form of such
 854 unidentifiabilities away from a point by following degenerate dimensions of the fisher information
 855 matrix [30]. Global structural non-identifiabilities can be found for models with polynomial or
 856 rational dynamics equations using DAISY [89], or through mean optimal transformations [90].
 857 With EPI, we have all the benefits given by a statistical inference method plus the ability to query
 858 the first- or second-order gradient of the probability of the inferred distribution at any chosen
 859 parameter value. The second-order gradient of the log probability (the Hessian), which is directly
 860 afforded by EPI distributions, produces quantified information about parametric sensitivity of the
 861 emergent property in parameter space (see Section 3.2).

862 **5.1.2 Deep probability distributions and normalizing flows**

863 Deep probability distributions are comprised of multiple layers of fully connected neural networks
 864 (Equation 13). When each neural network layer is restricted to be a bijective function, the sample
 865 density can be calculated using the change of variables formula at each layer of the network. For
 866 $\mathbf{z}_i = g_i(\mathbf{z}_{i-1})$,

$$p(\mathbf{z}_i) = p(g_i^{-1}(\mathbf{z}_i)) \left| \det \frac{\partial g_i^{-1}(\mathbf{z}_i)}{\partial \mathbf{z}_i} \right| = p(\mathbf{z}_{i-1}) \left| \det \frac{\partial g_i(\mathbf{z}_{i-1})}{\partial \mathbf{z}_{i-1}} \right|^{-1}. \quad (15)$$

867 However, this computation has cubic complexity in dimensionality for fully connected layers. By
 868 restricting our layers to normalizing flows [36, 37] – bijective functions with fast log determinant

869 Jacobian computations, which confer a fast calculation of the sample log probability. Fast log
870 probability calculation confers efficient optimization of the maximum entropy objective (see Section
871 5.1.4).

872 We use the real NVP [39] normalizing flow class, because its coupling architecture confers both
873 fast sampling (forward) and fast log probability evaluation (backward). Fast probability evaluation
874 facilitates fast gradient and Hessian evaluation of log probability throughout parameter space.
875 Glow permutations were used in between coupling stages [40]. This is in contrast to autoregressive
876 architectures [91, 92], in which only one of the forward or backward passes can be efficient. In this
877 work, normalizing flows are used as flexible parameter distribution approximations $q_{\theta}(\mathbf{z})$ having
878 weights and biases θ . We specify the architecture used in each application by the number of real
879 NVP affine coupling stages, and the number of neural network layers and units per layer of the
880 conditioning functions.

881 When calculating Hessians of log probabilities in deep probability distributions, it is important to
882 consider the normalizing flow architecture. With autoregressive architectures [91, 92], fast sam-
883 pling and fast log probability evaluations are mutually exclusive. That makes these architectures
884 undesirable for EPI, where efficient sampling is important for optimization, and log probability
885 evaluation speed predicates the efficiency of gradient and Hessian calculations. With real NVP
886 coupling architectures, we get both fast sampling and fast Hessians making both optimization and
887 scientific analysis efficient.

888 5.1.3 Maximum entropy distributions and exponential families

889 The inferred distribution of EPI is a maximum entropy distribution, which have fundamental links
890 to exponential family distributions. A maximum entropy distribution of form:

$$p^*(\mathbf{z}) = \underset{p \in \mathcal{P}}{\operatorname{argmax}} H(p(\mathbf{z})) \quad (16)$$

s.t. $\mathbb{E}_{\mathbf{z} \sim p}[T(\mathbf{z})] = \boldsymbol{\mu}_{\text{opt}},$

891 where $T(\mathbf{z})$ is the sufficient statistics vector and $\boldsymbol{\mu}_{\text{opt}}$ a vector of their mean values, will have
892 probability density in the exponential family:

$$p^*(\mathbf{z}) \propto \exp(\boldsymbol{\eta}^\top T(\mathbf{z})). \quad (17)$$

893 The mappings between the mean parameterization $\boldsymbol{\mu}_{\text{opt}}$ and the natural parameterization $\boldsymbol{\eta}$ are
894 formally hard to identify except in special cases [85].

895 In this manuscript, emergent properties are defined by statistics $f(\mathbf{x}; \mathbf{z})$ having a fixed mean $\boldsymbol{\mu}$ and
 896 variance σ^2 as in Equation 12. The variance constraint is a second moment constraint on $f(\mathbf{x}; \mathbf{z})$:

$$\text{Var}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] = \mathbb{E}_{\mathbf{z}, \mathbf{x}} [(f(\mathbf{x}; \mathbf{z}) - \boldsymbol{\mu})^2]. \quad (18)$$

897 As a general maximum entropy distribution (Equation 16), the sufficient statistics vector contains
 898 both first and second order moments of $f(\mathbf{x}; \mathbf{z})$

$$T(\mathbf{z}) = \begin{bmatrix} \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [f(\mathbf{x}; \mathbf{z})] \\ \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [(f(\mathbf{x}; \mathbf{z}) - \boldsymbol{\mu})^2] \end{bmatrix}, \quad (19)$$

899 which are constrained to the chosen means and variances

$$\boldsymbol{\mu}_{\text{opt}} = \begin{bmatrix} \boldsymbol{\mu} \\ \sigma^2 \end{bmatrix}. \quad (20)$$

900 Thus, $\boldsymbol{\mu}_{\text{opt}}$ is used to denote the mean parameter of the maximum entropy distribution defined by
 901 the emergent property (all constraints), while $\boldsymbol{\mu}$ is only the mean of $f(\mathbf{x}; \mathbf{z})$. The subscript “opt” of
 902 $\boldsymbol{\mu}_{\text{opt}}$ is chosen since it contains all of the constraint values to which the EPI optimization algorithm
 903 must adhere.

904 5.1.4 Augmented lagrangian optimization

905 To optimize $q_{\boldsymbol{\theta}}(\mathbf{z})$ in Equation 14, the constrained maximum entropy optimization is executed using
 906 the augmented lagrangian method. The following objective is minimized:

$$L(\boldsymbol{\theta}; \boldsymbol{\eta}_{\text{opt}}, c) = -H(q_{\boldsymbol{\theta}}) + \boldsymbol{\eta}_{\text{opt}}^\top R(\boldsymbol{\theta}) + \frac{c}{2} \|R(\boldsymbol{\theta})\|^2 \quad (21)$$

907 where there are average constraint violations

$$R(\boldsymbol{\theta}) = \mathbb{E}_{\mathbf{z} \sim q_{\boldsymbol{\theta}}(\mathbf{z})} [T(\mathbf{z}) - \boldsymbol{\mu}_{\text{opt}}], \quad (22)$$

908 $\boldsymbol{\eta}_{\text{opt}} \in \mathbb{R}^m$ are the lagrange multipliers where m is the number of total constraints

$$m = |\boldsymbol{\mu}_{\text{opt}}| = |T(\mathbf{z})| = 2|f(\mathbf{x}; \mathbf{z})|, \quad (23)$$

909 and c is the penalty coefficient. The mean parameter $\boldsymbol{\mu}_{\text{opt}}$ and sufficient statistics $T(\mathbf{z})$ are de-
 910 termined by the means $\boldsymbol{\mu}$ and variances σ^2 of the emergent property statistics $f(\mathbf{x}; \mathbf{z})$ defined in
 911 Equation 14. Specifically, $T(\mathbf{z})$ is a concatenation of the first and second moments (Equation 19)
 912 and $\boldsymbol{\mu}_{\text{opt}}$ is a concatenation of their constraints $\boldsymbol{\mu}$ and σ^2 (Equation 20). (Although, note that

913 this algorithm is written for general $T(\mathbf{z})$ and $\boldsymbol{\mu}_{\text{opt}}$ to satisfy the more general class of emergent
 914 properties.) The lagrange multipliers $\boldsymbol{\eta}_{\text{opt}}$ are closely related to the natural parameters $\boldsymbol{\eta}$ of expo-
 915 nential families (see Section 5.1.6). Weights and biases $\boldsymbol{\theta}$ of the deep probability distribution are
 916 optimized according to Equation 21 using the Adam optimizer with learning rate 10^{-3} [93].

917 The gradient with respect to entropy $H(q_{\boldsymbol{\theta}}(\mathbf{z}))$ can be expressed using the reparameterization trick
 918 as an expectation of the negative log density of parameter samples \mathbf{z} over the randomness in the
 919 parameterless initial distribution $q_0(\mathbf{z}_0)$:

$$H(q_{\boldsymbol{\theta}}(\mathbf{z})) = \int -q_{\boldsymbol{\theta}}(\mathbf{z}) \log(q_{\boldsymbol{\theta}}(\mathbf{z})) d\mathbf{z} = \mathbb{E}_{\mathbf{z} \sim q_{\boldsymbol{\theta}}} [-\log(q_{\boldsymbol{\theta}}(\mathbf{z}))] = \mathbb{E}_{\mathbf{z}_0 \sim q_0} [-\log(q_{\boldsymbol{\theta}}(g_{\boldsymbol{\theta}}(\mathbf{z}_0)))]. \quad (24)$$

920 Thus, the gradient of the entropy of the deep probability distribution can be estimated as an
 921 average of gradients with respect to the base distribution \mathbf{z}_0 :

$$\nabla_{\boldsymbol{\theta}} H(q_{\boldsymbol{\theta}}(\mathbf{z})) = \mathbb{E}_{\mathbf{z}_0 \sim q_0} [-\nabla_{\boldsymbol{\theta}} \log(q_{\boldsymbol{\theta}}(g_{\boldsymbol{\theta}}(\mathbf{z}_0)))]. \quad (25)$$

922 The gradients of the log density of the deep probability distribution are tractable through the use
 923 of normalizing flows (see Section 5.1.2).

924 The full EPI optimization algorithm is detailed in Algorithm 1. The lagrangian parameters $\boldsymbol{\eta}_{\text{opt}}$
 925 are initialized to zero and adapted following each augmented lagrangian epoch, which is a period of
 926 optimization with fixed $(\boldsymbol{\eta}_{\text{opt}}, c)$ for a given number of stochastic gradient descent (SGD) iterations.
 927 A low value of c is used initially, and conditionally increased after each epoch based on constraint
 928 error reduction. The penalty coefficient is updated based on the result of a hypothesis test regarding
 929 the reduction in constraint violation. The p-value of $\mathbb{E}[|R(\boldsymbol{\theta}_{k+1})|] > \gamma \mathbb{E}[|R(\boldsymbol{\theta}_k)|]$ is computed,
 930 and c_{k+1} is updated to βc_k with probability $1 - p$. The other update rule is $\boldsymbol{\eta}_{\text{opt},k+1} = \boldsymbol{\eta}_{\text{opt},k} +$
 931 $c_k \frac{1}{n} \sum_{i=1}^n (T(\mathbf{z}^{(i)}) - \boldsymbol{\mu}_{\text{opt}})$ given a batch size n and $\mathbf{z}^{(i)} \sim q_{\boldsymbol{\theta}}(\mathbf{z})$. Throughout the study, $\gamma = 0.25$,
 932 while β was chosen to be either 2 or 4. The batch size of EPI also varied according to application.

933 In general, c and $\boldsymbol{\eta}_{\text{opt}}$ should start at values encouraging entropic growth early in optimization.
 934 With each training epoch in which the update rule for c is invoked, the constraint satisfaction
 935 terms are increasingly weighted, which generally results in decreased entropy (e.g. see Figure
 936 S1C). This encourages the discovery of suitable regions of parameter space, and the subsequent
 937 refinement of the distribution to produce the emergent property. The momentum parameters of the
 938 Adam optimizer are reset at the end of each augmented lagrangian epoch, which proceeds for i_{max}
 939 iterations. In this work, we used a maximum number of augmented lagrangian epochs $k_{\text{max}} >= 5$.
 940 Rather than starting optimization from some $\boldsymbol{\theta}$ drawn from a randomized distribution, we found
 941 that initializing $q_{\boldsymbol{\theta}}(\mathbf{z})$ to approximate an isotropic gaussian distribution conferred more stable, con-

Algorithm 1: Emergent property inference

```

1 initialize  $\boldsymbol{\theta}$  by fitting  $q_{\boldsymbol{\theta}}$  to an isotropic gaussian of mean  $\boldsymbol{\mu}_{\text{init}}$  and variance  $\sigma_{\text{init}}^2$ 
2 initialize  $c_0 > 0$  and  $\boldsymbol{\eta}_{\text{opt},0} = \mathbf{0}$ .
3 for Augmented lagrangian epoch  $k = 1, \dots, k_{\max}$  do
4   for SGD iteration  $i = 1, \dots, i_{\max}$  do
5     Sample  $\mathbf{z}_0^{(1)}, \dots, \mathbf{z}_0^{(n)} \sim q_0$ , get transformed variable  $\mathbf{z}^{(j)} = g_{\boldsymbol{\theta}}(\mathbf{z}_0^{(j)})$ ,  $j = 1, \dots, n$ 
6     Update  $\boldsymbol{\theta}$  by descending its stochastic gradient (using ADAM optimizer [93]).  


$$\begin{aligned}\nabla_{\boldsymbol{\theta}} L(\boldsymbol{\theta}; \boldsymbol{\eta}_{\text{opt},k}, c) = & \frac{1}{n} \sum_{j=1}^n \nabla_{\boldsymbol{\theta}} \log q_{\boldsymbol{\theta}}(\mathbf{z}^{(j)}) + \frac{1}{n} \sum_{j=1}^n \nabla_{\boldsymbol{\theta}} \left( T(\mathbf{z}^{(j)}) - \boldsymbol{\mu}_{\text{opt}} \right) \boldsymbol{\eta}_{\text{opt},k} \\ & + c_k \frac{2}{n} \sum_{j=1}^{\frac{n}{2}} \nabla_{\boldsymbol{\theta}} \left( T(\mathbf{z}^{(j)}) - \boldsymbol{\mu}_{\text{opt}} \right) \cdot \frac{2}{n} \sum_{j=\frac{n}{2}+1}^n \left( T(\mathbf{z}^{(j)}) - \boldsymbol{\mu}_{\text{opt}} \right)\end{aligned}$$

7   end
8   Sample  $\mathbf{z}_0^{(1)}, \dots, \mathbf{z}_0^{(n)} \sim q_0$ , get transformed variable  $\mathbf{z}^{(j)} = g_{\boldsymbol{\theta}}(\mathbf{z}_0^{(j)})$ ,  $j = 1, \dots, n$ 
9   Update  $\boldsymbol{\eta}_{\text{opt},k+1} = \boldsymbol{\eta}_{\text{opt},k} + c_k \frac{1}{n} \sum_{j=1}^n (T(\mathbf{z}^{(j)}) - \boldsymbol{\mu}_{\text{opt}})$ .
10  Update  $c_{k+1} > c_k$  (see text for detail).
11 end

```

942 sistent optimization. The parameters of the gaussian initialization were chosen on an application-
 943 specific basis. Throughout the study, we chose isotropic Gaussian initializations with mean μ_{init} at
 944 the center of the support of the distribution and some variance σ_{init}^2 , except for one case, where an
 945 initialization informed by random search was used (see Section 5.2). Deep probability distributions
 946 were fit to these gaussian initializations using 10,000 iterations of stochastic gradient descent on
 947 the evidence lower bound (as in [86]) with Adam optimizer and a learning rate of 10^{-3} .

948 To assess whether the EPI distribution $q_{\theta}(\mathbf{z})$ produces the emergent property, we assess whether
 949 each individual constraint on the means and variances of $f(\mathbf{x}; \mathbf{z})$ is satisfied. We consider the EPI
 950 to have converged when a null hypothesis test of constraint violations $R(\boldsymbol{\theta})_i$ being zero is accepted
 951 for all constraints $i \in \{1, \dots, m\}$ at a significance threshold $\alpha = 0.05$. This significance threshold is
 952 adjusted through Bonferroni correction according to the number of constraints m . The p-values for
 953 each constraint are calculated according to a two-tailed nonparametric test, where 200 estimations
 954 of the sample mean $R(\boldsymbol{\theta})^i$ are made using N_{test} samples of $\mathbf{z} \sim q_{\theta}(\mathbf{z})$ at the end of the augmented
 955 lagrangian epoch. Of all k_{\max} augmented lagrangian epochs, we select the EPI inferred distribution
 956 as that which satisfies the convergence criteria and has greatest entropy.

957 When assessing the suitability of EPI for a particular modeling question, there are some important
 958 technical considerations. First and foremost, as in any optimization problem, the defined emergent
 959 property should always be appropriately conditioned (constraints should not have wildly different
 960 units). Furthermore, if the program is underconstrained (not enough constraints), the distribution
 961 grows (in entropy) unstably unless mapped to a finite support. If overconstrained, there is no
 962 parameter set producing the emergent property, and EPI optimization will fail (appropriately).

963 5.1.5 Example: 2D LDS

964 To gain intuition for EPI, consider a two-dimensional linear dynamical system (2D LDS) model
 965 (Fig. S1A):

$$\tau \frac{d\mathbf{x}}{dt} = A\mathbf{x} \quad (26)$$

966 with

$$A = \begin{bmatrix} a_{1,1} & a_{1,2} \\ a_{2,1} & a_{2,2} \end{bmatrix}. \quad (27)$$

967 To run EPI with the dynamics matrix elements as the free parameters $\mathbf{z} = [a_{1,1}, a_{1,2}, a_{2,1}, a_{2,2}]$
 968 (fixing $\tau = 1s$), the emergent property statistics $f(\mathbf{x}; \mathbf{z})$ were chosen to contain parts of the primary

969 eigenvalue of A , which predicate frequency, $\text{imag}(\lambda_1)$, and the growth/decay, $\text{real}(\lambda_1)$, of the system

$$f(\mathbf{x}; \mathbf{z}) \triangleq \begin{bmatrix} \text{real}(\lambda_1)(\mathbf{x}; \mathbf{z}) \\ \text{imag}(\lambda_1)(\mathbf{x}; \mathbf{z}) \end{bmatrix} \quad (28)$$

970 λ_1 is the eigenvalue of greatest real part when the imaginary component is zero, and alternatively
 971 that of positive imaginary component when the eigenvalues are complex conjugate pairs. To learn
 972 the distribution of real entries of A that produce a band of oscillating systems around 1Hz, we for-
 973 malized this emergent property as $\text{real}(\lambda_1)$ having mean zero with variance 0.25^2 , and the oscillation
 974 frequency $\frac{\text{imag}(\lambda_1)}{2\pi}$ having mean 1Hz with variance 0.1Hz^2 :

$$\begin{aligned} \mathcal{X} : \mathbb{E}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] &\triangleq \mathbb{E}_{\mathbf{z}, \mathbf{x}} \begin{bmatrix} \text{real}(\lambda_1)(\mathbf{x}; \mathbf{z}) \\ \text{imag}(\lambda_1)(\mathbf{x}; \mathbf{z}) \end{bmatrix} = \begin{bmatrix} 0 \\ 2\pi \end{bmatrix} \triangleq \boldsymbol{\mu} \\ \text{Var}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] &\triangleq \text{Var}_{\mathbf{z}, \mathbf{x}} \begin{bmatrix} \text{real}(\lambda_1)(\mathbf{x}; \mathbf{z}) \\ \text{imag}(\lambda_1)(\mathbf{x}; \mathbf{z}) \end{bmatrix} = \begin{bmatrix} 0.25^2 \\ (\frac{\pi}{5})^2 \end{bmatrix} \triangleq \boldsymbol{\sigma}^2. \end{aligned} \quad (29)$$

975 To write the emergent property \mathcal{X} in the form required for the augmented lagrangian optimization
 976 (Section 5.1.4), we concatenate these first and second moment constraints into a vector of sufficient
 977 statistics $T(\mathbf{z})$ and constraint values $\boldsymbol{\mu}_{\text{opt}}$.

$$\mathbb{E}_{\mathbf{z}} [T(\mathbf{z})] \triangleq \mathbb{E}_{\mathbf{z}} \begin{bmatrix} \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [\text{real}(\lambda_1)(\mathbf{x}; \mathbf{z})] \\ \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [\text{imag}(\lambda_1)(\mathbf{x}; \mathbf{z})] \\ \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [(\text{real}(\lambda_1)(\mathbf{x}; \mathbf{z}) - 0)^2] \\ \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [(\text{imag}(\lambda_1)(\mathbf{x}; \mathbf{z}) - 2\pi)^2] \end{bmatrix} = \begin{bmatrix} 0 \\ 2\pi \\ 0.25^2 \\ (\frac{\pi}{5})^2 \end{bmatrix} \triangleq \boldsymbol{\mu}_{\text{opt}}. \quad (30)$$

978 From now on in all scientific applications (Sections 5.2-5.5, we specify how the EPI optimization
 979 was setup by specifying $f(\mathbf{x}; \mathbf{z})$, $\boldsymbol{\mu}$, and $\boldsymbol{\sigma}^2$.

980 Unlike the models we presented in the main text, this model admits an analytical form for the
 981 mean emergent property statistics given parameter \mathbf{z} , since the eigenvalues can be calculated using
 982 the quadratic formula:

$$\lambda = \frac{(\frac{a_{1,1}+a_{2,2}}{\tau}) \pm \sqrt{(\frac{a_{1,1}+a_{2,2}}{\tau})^2 + 4(\frac{a_{1,2}a_{2,1}-a_{1,1}a_{2,2}}{\tau})}}{2}. \quad (31)$$

983 We study this example, because the inferred distribution is curved and multimodal, and we can
 984 compare the result of EPI to analytically derived contours of the emergent property statistics.

985 Despite the simple analytic form of the emergent property statistics, the EPI distribution in this
 986 example is not simply determined. Although $\mathbb{E}_{\mathbf{z}} [T(\mathbf{z})]$ is calculable directly via a closed form

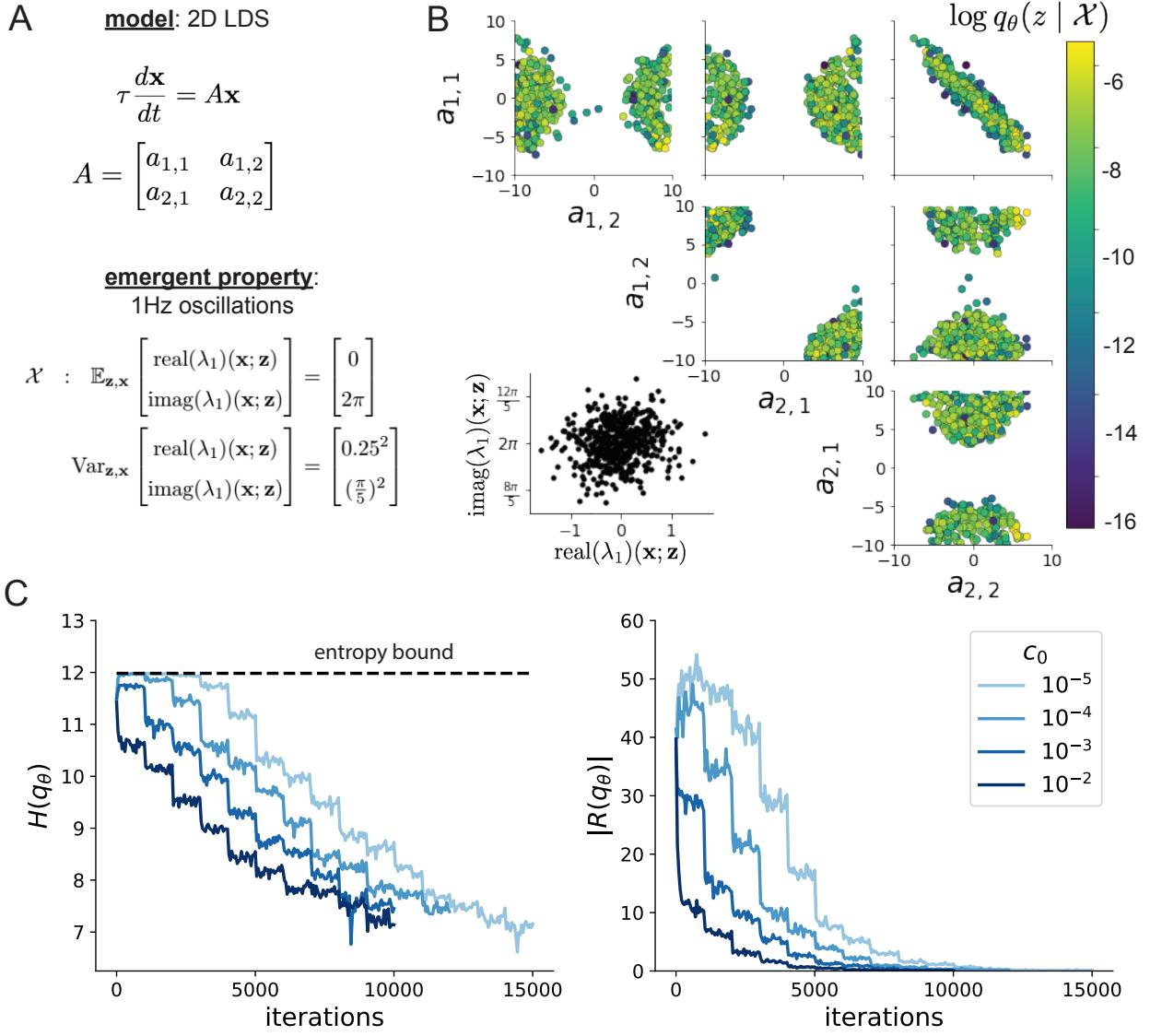


Figure S1: **A.** Two-dimensional linear dynamical system model, where real entries of the dynamics matrix A are the parameters. **B.** The EPI distribution for a two-dimensional linear dynamical system with $\tau = 1$ that produces an average of 1Hz oscillations with some small amount of variance. Dashed lines indicate the parameter axes. **C.** Entropy throughout the optimization. At the beginning of each augmented lagrangian epoch ($i_{\max} = 2,000$ iterations), the entropy dipped due to the shifted optimization manifold where emergent property constraint satisfaction is increasingly weighted. **D.** Emergent property moments throughout optimization. At the beginning of each augmented lagrangian epoch, the emergent property moments adjust closer to their constraints.

987 function, the distribution $q_{\theta}^*(\mathbf{z} \mid \mathcal{X})$ cannot be derived directly. This fact is due to the formally hard
 988 problem of the backward mapping: finding the natural parameters $\boldsymbol{\eta}$ from the mean parameters $\boldsymbol{\mu}$
 989 of an exponential family distribution [85]. Instead, we used EPI to approximate this distribution
 990 (Fig. S1B). We used a real NVP normalizing flow architecture three coupling layers and two-layer
 991 neural networks of 50 units per layer, mapped onto a support of $z_i \in [-10, 10]$. (see Section 5.1.2).

992 Even this relatively simple system has nontrivial (though intuitively sensible) structure in the
 993 parameter distribution. To validate our method, we analytically derived the contours of the proba-
 994 bility density from the emergent property statistics and values. In the $a_{1,1}$ - $a_{2,2}$ plane, the black line
 995 at $\text{real}(\lambda_1) = \frac{a_{1,1} + a_{2,2}}{2} = 0$, dashed black line at the standard deviation $\text{real}(\lambda_1) = \frac{a_{1,1} + a_{2,2}}{2} \pm 0.25$,
 996 and the dashed gray line at twice the standard deviation $\text{real}(\lambda_1) = \frac{a_{1,1} + a_{2,2}}{2} \pm 0.5$ follow the con-
 997 tour of probability density of the samples (Fig. S2A). The distribution precisely reflects the desired
 998 statistical constraints and model degeneracy in the sum of $a_{1,1}$ and $a_{2,2}$. Intuitively, the parameters
 999 equivalent with respect to emergent property statistic $\text{real}(\lambda_1)$ have similar log densities.

1000 To explain the bimodality of the EPI distribution, we examined the imaginary component of λ_1 .
 1001 When $\text{real}(\lambda_1) = a_{1,1} + a_{2,2} = 0$ (which is the case on average in \mathcal{X}), we have

$$\text{imag}(\lambda_1) = \begin{cases} \sqrt{\frac{a_{1,1}a_{2,2} - a_{1,2}a_{2,1}}{\tau}}, & \text{if } a_{1,1}a_{2,2} < a_{1,2}a_{2,1} \\ 0 & \text{otherwise} \end{cases}. \quad (32)$$

1002 In Figure S2B, we plot the contours of $\text{imag}(\lambda_1)$ where $a_{1,1}a_{2,2}$ is fixed to 0 at one standard
 1003 deviation ($\frac{\pi}{5}$, black dashed) and two standard deviations ($\frac{2\pi}{5}$, gray dashed) from the mean of 2π .
 1004 This validates the curved multimodal structure of the inferred distribution learned through EPI.
 1005 Subtler combinations of model and emergent property will have more complexity, further motivating
 1006 the use of EPI for understanding these systems. As we expect, the distribution results in samples
 1007 of two-dimensional linear systems oscillating near 1Hz (Fig. S3).

1008 5.1.6 EPI as variational inference

1009 In variational inference, a posterior approximation q_{θ}^* is chosen from within some variational family
 1010 \mathcal{Q} to be as close as possible to the posterior under the KL divergence criteria

$$q_{\theta}^*(\mathbf{z}) = \underset{q_{\theta} \in \mathcal{Q}}{\operatorname{argmin}} KL(q_{\theta}(\mathbf{z}) \parallel p(\mathbf{z} \mid \mathbf{x})). \quad (33)$$

1011 This KL divergence can be written in terms of entropy of the variational approximation:

$$KL(q_{\theta}(\mathbf{z}) \parallel p(\mathbf{z} \mid \mathbf{x})) = \mathbb{E}_{\mathbf{z} \sim q_{\theta}} [\log(q_{\theta}(\mathbf{z}))] - \mathbb{E}_{\mathbf{z} \sim q_{\theta}} [\log(p(\mathbf{z} \mid \mathbf{x}))] \quad (34)$$

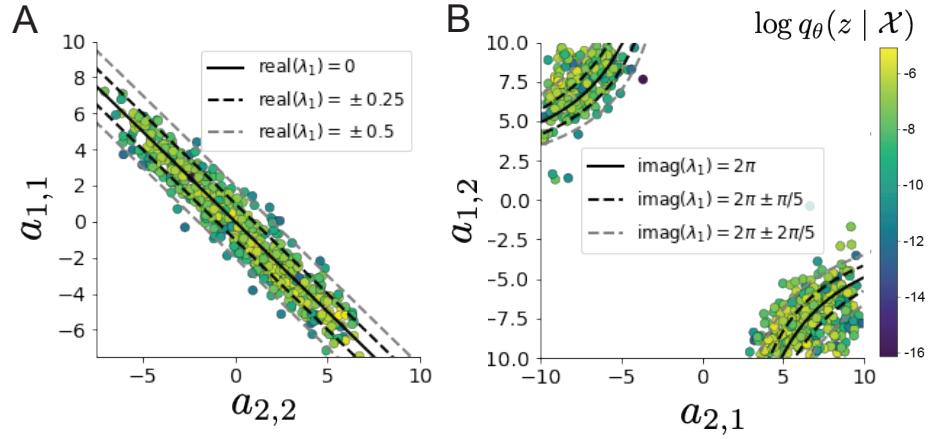


Figure S2: **A.** Probability contours in the $a_{1,1}$ - $a_{2,2}$ plane were derived from the relationship to emergent property statistic of growth/decay factor $\text{real}(\lambda_1)$. **B.** Probability contours in the $a_{1,2}$ - $a_{2,1}$ plane were derived from the emergent property statistic of oscillation frequency $2\pi\text{imag}(\lambda_1)$.

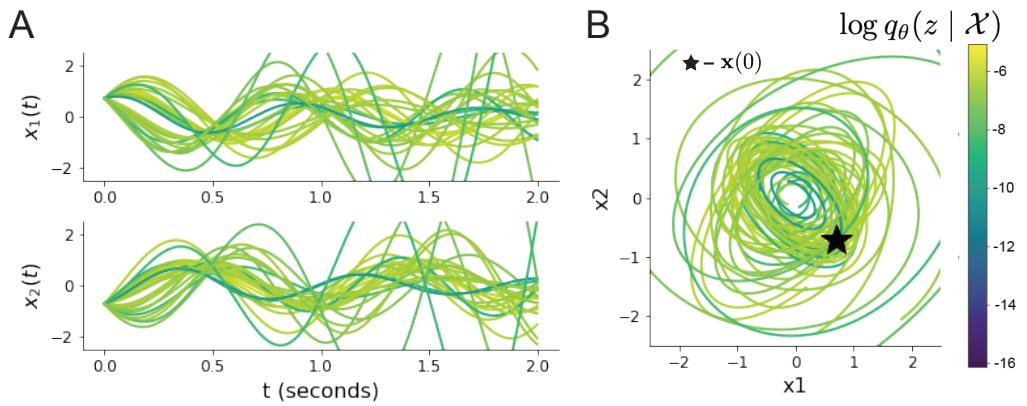


Figure S3: Sampled dynamical systems $\mathbf{z} \sim q_{\theta}(\mathbf{z} | \mathcal{X})$ and their simulated activity from $\mathbf{x}(t = 0) = [\frac{\sqrt{2}}{2}, -\frac{\sqrt{2}}{2}]$ colored by log probability. **A.** Each dimension of the simulated trajectories throughout time. **B.** The simulated trajectories in phase space.

1012

$$= -H(q_{\theta}) - \mathbb{E}_{\mathbf{z} \sim q_{\theta}} [\log(p(\mathbf{x} | \mathbf{z})) + \log(p(\mathbf{z})) - \log(p(\mathbf{x}))] \quad (35)$$

1013 Since the marginal distribution of the data $p(\mathbf{x})$ (or ‘‘evidence’’) is independent of θ , variational
 1014 inference is executed by optimizing the remaining expression. This is usually framed as maximizing
 1015 the evidence lower bound (ELBO)

$$\operatorname{argmin}_{q_{\theta} \in Q} KL(q_{\theta} || p(\mathbf{z} | \mathbf{x})) = \operatorname{argmax}_{q_{\theta} \in Q} H(q_{\theta}) + \mathbb{E}_{\mathbf{z} \sim q_{\theta}} [\log(p(\mathbf{x} | \mathbf{z})) + \log(p(\mathbf{z}))]. \quad (36)$$

1016 Now, we will show how the maximum entropy problem of EPI is equivalent to variational inference.

1017 In general, a maximum entropy problem (as in Equation 16) has an equivalent lagrange dual form:

$$\begin{aligned} \operatorname{argmax}_{q \in \mathcal{Q}} H(q(\mathbf{z})) &\iff \operatorname{argmax}_{q \in \mathcal{Q}} H(q(\mathbf{z})) + \boldsymbol{\eta}^{*\top} \mathbb{E}_{\mathbf{z} \sim q} [T(\mathbf{z})], \\ \text{s.t. } \mathbb{E}_{\mathbf{z} \sim q} [T(\mathbf{z})] &= \mathbf{0} \end{aligned} \quad (37)$$

1018 with lagrange multipliers $\boldsymbol{\eta}^*$. By moving the lagrange multipliers within the expectation

$$q^* = \operatorname{argmax}_{q \in \mathcal{Q}} H(q(\mathbf{z})) + \mathbb{E}_{\mathbf{z} \sim q} [\boldsymbol{\eta}^{*\top} T(\mathbf{z})], \quad (38)$$

1019 inserting a $\log \exp(\cdot)$ within the expectation,

$$q^* = \operatorname{argmax}_{q \in \mathcal{Q}} H(q(\mathbf{z})) + \mathbb{E}_{\mathbf{z} \sim q} \left[\log \exp \left(\boldsymbol{\eta}^{*\top} T(\mathbf{z}) \right) \right], \quad (39)$$

1020 and finally choosing $T(\cdot)$ to be likelihood averaged statistics as in EPI

$$q^* = \operatorname{argmax}_{q \in \mathcal{Q}} H(q(\mathbf{z})) + \mathbb{E}_{\mathbf{z} \sim q} \left[\log \exp \left(\boldsymbol{\eta}^{*\top} \begin{bmatrix} \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [\phi_1(\mathbf{x}; \mathbf{z})] \\ \dots \\ \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [\phi_m(\mathbf{x}; \mathbf{z})] \end{bmatrix} \right) \right], \quad (40)$$

1021 we can compare directly to the objective used in variational inference (Equation 36). We see
 1022 that EPI is exactly variational inference with an exponential family likelihood defined by sufficient
 1023 statistics $T(\mathbf{z}) = \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [\phi(\mathbf{x}; \mathbf{z})]$, and where the natural parameter $\boldsymbol{\eta}^*$ is predicated by the mean
 1024 parameter $\boldsymbol{\mu}_{\text{opt}}$. Equation 40 implies that EPI uses an improper (or uniform) prior, which is easily
 1025 changed.

1026 This derivation of the equivalence between EPI and variational inference emphasizes why defining
 1027 a statistical inference program by its mean parameterization $\boldsymbol{\mu}_{\text{opt}}$ is so useful. With EPI, one can
 1028 clearly define the emergent property \mathcal{X} that the model of interest should produce through intuitive
 1029 selection of $\boldsymbol{\mu}_{\text{opt}}$ for a given $T(\mathbf{z})$. Alternatively, figuring out the correct natural parameters $\boldsymbol{\eta}^*$ for
 1030 the same $T(\mathbf{z})$ that produces \mathcal{X} is a formally hard problem.

1031 **5.2 Stomatogastric ganglion**

1032 In Section 3.1 and 3.2, we used EPI to infer conductance parameters in a model of the stomatogastric
 1033 ganglion (STG) [41]. This 5-neuron circuit model represents two subcircuits: that generating the
 1034 pyloric rhythm (fast population) and that generating the gastric mill rhythm (slow population).
 1035 The additional neuron (the IC neuron of the STG) receives inhibitory synaptic input from both
 1036 subcircuits, and can couple to either rhythm dependent on modulatory conditions. There is also
 1037 a parametric regime in which this neuron fires at an intermediate frequency between that of the
 1038 fast and slow populations [41], which we infer with EPI as a motivational example. This model
 1039 is not to be confused with an STG subcircuit model of the pyloric rhythm [68], which has been
 1040 statistically inferred in other studies [15, 35].

1041 **5.2.1 STG model**

1042 We analyze how the parameters $\mathbf{z} = [g_{el}, g_{synA}]$ govern the emergent phenomena of intermediate
 1043 hub frequency in a model of the stomatogastric ganglion (STG) [41] shown in Figure 1A with
 1044 activity $\mathbf{x} = [x_{f1}, x_{f2}, x_{hub}, x_{s1}, x_{s2}]$, using the same hyperparameter choices as Gutierrez et al.
 1045 Each neuron's membrane potential $x_\alpha(t)$ for $\alpha \in \{f1, f2, hub, s1, s2\}$ is the solution of the following
 1046 stochastic differential equation:

$$C_m \frac{dx_\alpha}{dt} = -[h_{leak}(\mathbf{x}; \mathbf{z}) + h_{Ca}(\mathbf{x}; \mathbf{z}) + h_K(\mathbf{x}; \mathbf{z}) + h_{hyp}(\mathbf{x}; \mathbf{z}) + h_{elec}(\mathbf{x}; \mathbf{z}) + h_{syn}(\mathbf{x}; \mathbf{z})] + dB. \quad (41)$$

1047 The input current of each neuron is the sum of the leak, calcium, potassium, hyperpolarization,
 1048 electrical and synaptic currents. Each current component is a function of all membrane potentials
 1049 and the conductance parameters \mathbf{z} . Finally, we include gaussian noise dB to the model of Gutierrez
 1050 et al. so that the model stochastic, although this is not required by EPI.

1051 The capacitance of the cell membrane was set to $C_m = 1nF$. Specifically, the currents are the
 1052 difference in the neuron's membrane potential and that current type's reversal potential multiplied
 1053 by a conductance:

$$h_{leak}(\mathbf{x}; \mathbf{z}) = g_{leak}(x_\alpha - V_{leak}) \quad (42)$$

$$h_{elec}(\mathbf{x}; \mathbf{z}) = g_{el}(x_\alpha^{post} - x_\alpha^{pre}) \quad (43)$$

$$h_{syn}(\mathbf{x}; \mathbf{z}) = g_{syn}S_\infty^{pre}(x_\alpha^{post} - V_{syn}) \quad (44)$$

$$h_{Ca}(\mathbf{x}; \mathbf{z}) = g_{Ca}M_\infty(x_\alpha - V_{Ca}) \quad (45)$$

1057

$$h_K(\mathbf{x}; \mathbf{z}) = g_K N(x_\alpha - V_K) \quad (46)$$

1058

$$h_{hyp}(\mathbf{x}; \mathbf{z}) = g_h H(x_\alpha - V_{hyp}). \quad (47)$$

1059 The reversal potentials were set to $V_{leak} = -40mV$, $V_{Ca} = 100mV$, $V_K = -80mV$, $V_{hyp} = -20mV$,
 1060 and $V_{syn} = -75mV$. The other conductance parameters were fixed to $g_{leak} = 1 \times 10^{-4}\mu S$. g_{Ca} ,
 1061 g_K , and g_{hyp} had different values based on fast, intermediate (hub) or slow neuron. The fast
 1062 conductances had values $g_{Ca} = 1.9 \times 10^{-2}$, $g_K = 3.9 \times 10^{-2}$, and $g_{hyp} = 2.5 \times 10^{-2}$. The intermediate
 1063 conductances had values $g_{Ca} = 1.7 \times 10^{-2}$, $g_K = 1.9 \times 10^{-2}$, and $g_{hyp} = 8.0 \times 10^{-3}$. Finally, the
 1064 slow conductances had values $g_{Ca} = 8.5 \times 10^{-3}$, $g_K = 1.5 \times 10^{-2}$, and $g_{hyp} = 1.0 \times 10^{-2}$.

1065 Furthermore, the Calcium, Potassium, and hyperpolarization channels have time-dependent gating
 1066 dynamics dependent on steady-state gating variables M_∞ , N_∞ and H_∞ , respectively:

$$M_\infty = 0.5 \left(1 + \tanh \left(\frac{x_\alpha - v_1}{v_2} \right) \right) \quad (48)$$

1067

$$\frac{dN}{dt} = \lambda_N (N_\infty - N) \quad (49)$$

1068

$$N_\infty = 0.5 \left(1 + \tanh \left(\frac{x_\alpha - v_3}{v_4} \right) \right) \quad (50)$$

1069

$$\lambda_N = \phi_N \cosh \left(\frac{x_\alpha - v_3}{2v_4} \right) \quad (51)$$

1070

$$\frac{dH}{dt} = \frac{(H_\infty - H)}{\tau_h} \quad (52)$$

1071

$$H_\infty = \frac{1}{1 + \exp \left(\frac{x_\alpha + v_5}{v_6} \right)} \quad (53)$$

1072

$$\tau_h = 272 - \left(\frac{-1499}{1 + \exp \left(\frac{-x_\alpha + v_7}{v_8} \right)} \right). \quad (54)$$

1073 where we set $v_1 = 0mV$, $v_2 = 20mV$, $v_3 = 0mV$, $v_4 = 15mV$, $v_5 = 78.3mV$, $v_6 = 10.5mV$,
 1074 $v_7 = -42.2mV$, $v_8 = 87.3mV$, $v_9 = 5mV$, and $v_{th} = -25mV$.

1075 Finally, there is a synaptic gating variable as well:

$$S_\infty = \frac{1}{1 + \exp \left(\frac{v_{th} - x_\alpha}{v_9} \right)}. \quad (55)$$

1076 When the dynamic gating variables are considered, this is actually a 15-dimensional nonlinear
 1077 dynamical system. The gaussian noise $d\mathbf{B}$ has variance $(1 \times 10^{-12})^2$ A², and introduces variability
 1078 in frequency at each parameterization \mathbf{z} .

1079 **5.2.2 Hub frequency calculation**

1080 In order to measure the frequency of the hub neuron during EPI, the STG model was simulated for
1081 $T = 300$ time steps of $dt = 25\text{ms}$. The chosen dt and T were the most computationally convenient
1082 choices yielding accurate frequency measurement. We used a basis of complex exponentials with
1083 frequencies from 0.0-1.0 Hz at 0.01Hz resolution to measure frequency from simulated time series

$$\Phi = [0.0, 0.01, \dots, 1.0]^\top \dots \quad (56)$$

1084 To measure spiking frequency, we processed simulated membrane potentials with a relu (spike
1085 extraction) and low-pass filter with averaging window of size 20, then took the frequency with the
1086 maximum absolute value of the complex exponential basis coefficients of the processed time-series.
1087 The first 20 temporal samples of the simulation are ignored to account for initial transients.

1088 To differentiate through the maximum frequency identification, we used a soft-argmax Let $X_\alpha \in$
1089 $\mathcal{C}^{|\Phi|}$ be the complex exponential filter bank dot products with the signal $x_\alpha \in \mathbb{R}^N$, where $\alpha \in$
1090 $\{f1, f2, \text{hub}, s1, s2\}$. The soft-argmax is then calculated using temperature parameter $\beta_\psi = 100$

$$\psi_\alpha = \text{softmax}(\beta_\psi |X_\alpha| \odot i), \quad (57)$$

1091 where $i = [0, 1, \dots, 100]$. The frequency is then calculated as

$$\omega_\alpha = 0.01\psi_\alpha \text{Hz}. \quad (58)$$

1092 Intermediate hub frequency, like all other emergent properties in this work, is defined by the mean
1093 and variance of the emergent property statistics. In this case, we have one statistic, hub neuron
1094 frequency, where the mean was chosen to be 0.55Hz,(Equation 2) and variance was chosen to be
1095 0.025^2 Hz 2 (Equation 3).

1096 **5.2.3 EPI details for the STG model**

1097 EPI was run for the STG model using

$$f(\mathbf{x}; \mathbf{z}) = \omega_{\text{hub}}(\mathbf{x}; \mathbf{z}), \quad (59)$$

1098

$$\boldsymbol{\mu} = \begin{bmatrix} 0.55 \end{bmatrix}, \quad (60)$$

1099 and

$$\boldsymbol{\sigma}^2 = \begin{bmatrix} 0.025^2 \end{bmatrix} \quad (61)$$

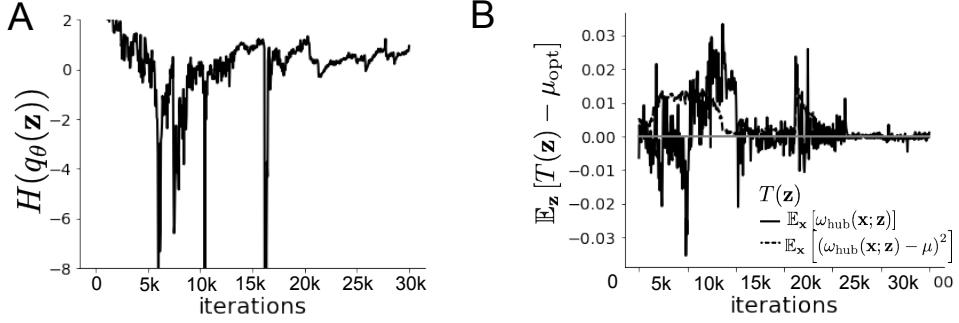


Figure S4: EPI optimization of the STG model producing network syncing. **A.** Entropy throughout optimization. **B.** The emergent property statistic means and variances converge to their constraints at 25,000 iterations following the fifth augmented lagrangian epoch.

(see Sections 5.1.3-5.1.4, and example in Section 5.1.5). Throughout optimization, the augmented lagrangian parameters η and c , were updated after each epoch of $i_{\max} = 5,000$ iterations (see Section 5.1.4). The optimization converged after five epochs (Fig. S4).

For EPI in Fig 1E, we used a real NVP architecture with three coupling layers and two-layer neural networks of 25 units per layer. The normalizing flow architecture mapped $\mathbf{z}_0 \sim \mathcal{N}(\mathbf{0}, I)$ to a support of $\mathbf{z} = [g_{\text{el}}, g_{\text{synA}}] \in [4, 8] \times [0.01, 4]$, initialized to a gaussian approximation of samples returned by a preliminary ABC search. We did not include $g_{\text{synA}} < 0.01$, for numerical stability. EPI optimization was run using 5 different random seeds for architecture initialization $\boldsymbol{\theta}$ with an augmented lagrangian coefficient of $c_0 = 10^5$, $\beta = 2$, a batch size $n = 400$, and we simulated one $\mathbf{x}^{(i)}$ per $\mathbf{z}^{(i)}$. The architecture converged with criteria $N_{\text{test}} = 100$.

5.2.4 Hessian sensitivity vectors

To quantify the second-order structure of the EPI distribution, we evaluated the Hessian of the log probability $\frac{\partial^2 \log q(\mathbf{z}|\mathcal{X})}{\partial \mathbf{z} \partial \mathbf{z}^\top}$. The eigenvector of this Hessian with most negative eigenvalue is defined as the sensitivity dimension \mathbf{v}_1 , and all subsequent eigenvectors are ordered by increasing eigenvalue. These eigenvalues are quantifications of how fast the emergent property deteriorates via the parameter combination of their associated eigenvector. In Figure 1D, the sensitivity dimension v_1 (solid) and the second eigenvector of the Hessian v_2 (dashed) are shown evaluated at the mode of the distribution. Since the Hessian eigenvectors have sign degeneracy, the visualized directions in 2-D parameter space were chosen to have positive g_{synA} . The length of the arrows is inversely proportional to the square root of the absolute value of their eigenvalues $\lambda_1 = -10.7$ and $\lambda_2 = -3.22$. For

1120 the same magnitude perturbation away from the mode, intermediate hub frequency only diminishes
 1121 along the sensitivity dimension \mathbf{v}_1 (Fig. 1E-F).

1122 5.3 Scaling EPI for stable amplification in RNNs

1123 5.3.1 Rank-2 RNN model

1124 We examined the scaling properties of EPI by learning connectivities of RNNs of increasing size
 1125 that exhibit stable amplification. Rank-2 RNN connectivity was modeled as $W = UV^\top$, where
 1126 $U = [\mathbf{U}_1 \ \mathbf{U}_2] + g\chi^{(W)}$, $V = [\mathbf{V}_1 \ \mathbf{V}_2] + g\chi^{(V)}$, and $\chi_{i,j}^{(W)}, \chi_{i,j}^{(V)} \sim \mathcal{N}(0, 1)$. This RNN model has
 1127 dynamics

$$\tau \dot{\mathbf{x}} = -\mathbf{x} + W\mathbf{x}. \quad (62)$$

1128 In this analysis, we inferred connectivity parameterizations $\mathbf{z} = [\mathbf{U}_1^\top, \mathbf{U}_2^\top, \mathbf{V}_1^\top, \mathbf{V}_2^\top]^\top \in [-1, 1]^{(4N)}$
 1129 that produced stable amplification using EPI, SMC-ABC [26], and SNPE [35] (see Section Related
 1130 Methods).

1131 5.3.2 Stable amplification

1132 For this RNN model to be stable, all real eigenvalues of W must be less than 1: $\text{real}(\lambda_1) < 1$,
 1133 where λ_1 denotes the greatest real eigenvalue of W . For a stable RNN to amplify at least one input
 1134 pattern, the symmetric connectivity $W^s = \frac{W+W^\top}{2}$ must have an eigenvalue greater than 1: $\lambda_1^s > 1$,
 1135 where λ^s is the maximum eigenvalue of W^s . These two conditions are necessary and sufficient for
 1136 stable amplification in RNNs [51].

1137 5.3.3 EPI details for RNNs

1138 We defined the emergent property of stable amplification with means of these eigenvalues (0.5
 1139 and 1.5, respectively) that satisfy these conditions. To complete the emergent property definition,
 1140 we chose variances (0.25²) about those means such that samples rarely violate the eigenvalue
 1141 constraints. To write the emergent property of Equation 5 in terms of the EPI optimization, we
 1142 have

$$f(\mathbf{x}; \mathbf{z}) = \begin{bmatrix} \text{real}(\lambda_1)(\mathbf{x}; \mathbf{z}) \\ \lambda_1^s(\mathbf{x}; \mathbf{z}) \end{bmatrix}, \quad (63)$$

1143

$$\boldsymbol{\mu} = \begin{bmatrix} 0.5 \\ 1.5 \end{bmatrix}, \quad (64)$$

1144 and

$$\boldsymbol{\sigma}^2 = \begin{bmatrix} 0.25^2 \\ 0.25^2 \end{bmatrix} \quad (65)$$

1145 (see Sections 5.1.3-5.1.4, and example in Section 5.1.5). Gradients of maximum eigenvalues of Her-
 1146 mitian matrices like W^s are available with modern automatic differentiation tools. To differentiate
 1147 through the $\text{real}(\lambda_1)$, we solved the following equation for eigenvalues of rank-2 matrices using the
 1148 rank reduced matrix $W^r = V^\top U$

$$\lambda_{\pm} = \frac{\text{Tr}(W^r) \pm \sqrt{\text{Tr}(W^r)^2 - 4\text{Det}(W^r)}}{2}. \quad (66)$$

1149 For EPI in Fig. 2, we used a real NVP architecture with three coupling layers of affine transfor-
 1150 mations parameterized by two-layer neural networks of 100 units per layer. The initial distribution
 1151 was a standard isotropic gaussian $\mathbf{z}_0 \sim \mathcal{N}(\mathbf{0}, I)$ mapped to the support of $\mathbf{z}_i \in [-1, 1]$. We used an
 1152 augmented lagrangian coefficient of $c_0 = 10^3$, a batch size $n = 200$, $\beta = 4$, and we simulated one
 1153 $\mathbf{W}^{(i)}$ per $\mathbf{z}^{(i)}$. We chose to use $i_{\max} = 500$ iterations per augmented lagrangian epoch and emergent
 1154 property constraint convergence was evaluated at $N_{\text{test}} = 200$ (Fig. 2B blue line, and Fig. 2C-D
 1155 blue). It was fastest to initialize the EPI distribution on a Tesla V100 GPU, and then subsequently
 1156 optimize it on a CPU with 32 cores. EPI timing measurements accounted for this initialization
 1157 period.

1158

5.3.4 Methodological comparison

1159 We compared EPI to two alternative simulation-based inference techniques, since the likelihood
 1160 of these eigenvalues given \mathbf{z} is not available. Approximate bayesian computation (ABC) [24] is a
 1161 rejection sampling technique for obtaining sets of parameters \mathbf{z} that produce activity \mathbf{x} close to some
 1162 observed data \mathbf{x}_0 . Sequential Monte Carlo approximate bayesian computation (SMC-ABC) is the
 1163 state-of-the-art ABC method, which leverages SMC techniques to improve sampling speed. We ran
 1164 SMC-ABC with the pyABC package [94] to infer RNNs with stable amplification: connectivities
 1165 having eigenvalues within an ϵ -defined l -2 distance of

$$\mathbf{x}_0 = \begin{bmatrix} \text{real}(\lambda_1) \\ \lambda_1^s \end{bmatrix} = \begin{bmatrix} 0.5 \\ 1.5 \end{bmatrix}. \quad (67)$$

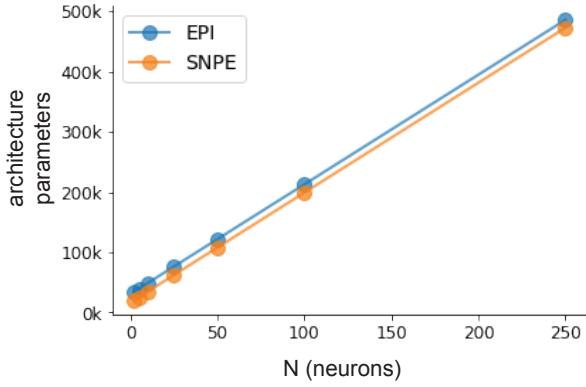


Figure S5: Number of parameters in deep probability distribution architectures of EPI (blue) and SNPE (orange) by RNN size (N).

1166 SMC-ABC was run with a uniform prior over $\mathbf{z} \in [-1, 1]^{(4N)}$, a population size of 1,000 particles
 1167 with simulations parallelized over 32 cores, and a multivariate normal transition model.

1168 SNPE, the next approach in our comparison, is far more similar to EPI. Like EPI, SNPE treats pa-
 1169 rameters in mechanistic models with deep probability distributions, yet the two learning algorithms
 1170 are categorically different. SNPE uses a two-network architecture to approximate the posterior dis-
 1171 tribution of the model conditioned on observed data \mathbf{x}_0 . The amortizing network maps observations
 1172 \mathbf{x}_i to the parameters of the deep probability distribution. The weights and biases of the parameter
 1173 network are optimized by sequentially augmenting the training data with additional pairs $(\mathbf{z}_i, \mathbf{x}_i)$
 1174 based on the most recent posterior approximation. This sequential procedure is important to get
 1175 training data \mathbf{z}_i to be closer to the true posterior, and \mathbf{x}_i to be closer to the observed data. For
 1176 the deep probability distribution architecture, we chose a masked autoregressive flow with affine
 1177 couplings (the default choice), three transforms, 50 hidden units, and a normalizing flow mapping
 1178 to the support as in EPI. This architectural choice closely tracked the size of the architecture used
 1179 by EPI (Fig. S5). As in SMC-ABC, we ran SNPE with $\mathbf{x}_0 = \mu$. All SNPE optimizations were run
 1180 for a limit of 1.5 days, or until two consecutive rounds resulted in a validation log probability lower
 1181 than the maximum observed for that random seed. It was always faster to run SNPE on a CPU
 1182 with 32 cores rather than on a Tesla V100 GPU.

1183 To compare the efficiency of these algorithms for inferring RNN connectivity distributions producing
 1184 stable amplification, we develop a convergence criteria that can be used across methods. While EPI
 1185 has its own hypothesis testing convergence criteria for the emergent property, it would not make
 1186 sense to use this criteria on SNPE and SMC-ABC which do not constrain the means and variances

1187 of their predictions. Instead, we consider EPI and SNPE to have converged after completing its
1188 most recent optimization epoch (EPI) or round (SNPE) in which the distance $\|\mathbb{E}_{\mathbf{z}, \mathbf{x}} [f(\mathbf{x}; \mathbf{z})] - \boldsymbol{\mu}\|_2$
1189 is less than 0.5. We consider SMC-ABC to have converged once the population produces samples
1190 within the $\epsilon = 0.5$ ball ensuring stable amplification.

1191 When assessing the scalability of SNPE, it is important to check that alternative hyperparameter-
1192izations could not yield better performance. Key hyperparameters of the SNPE optimization are
1193 the number of simulations per round n_{round} , the number of atoms used in the atomic proposals of
1194 the SNPE-C algorithm [95], and the batch size n . To match EPI, we used a batch size of $n = 200$
1195 for $N \leq 25$, however we found $n = 1,000$ to be helpful for SNPE in higher dimensions. While
1196 $n_{\text{round}} = 1,000$ yielded SNPE convergence for $N \leq 25$, we found that a substantial increase to
1197 $n_{\text{round}} = 25,000$ yielded more consistent convergence at $N = 50$ (Fig. S6A). By increasing n_{round} ,
1198 we also necessarily increase the duration of each round. At $N = 100$, we tried two hyperparameter
1199 modifications. As suggested in [95], we increased n_{atom} by an order of magnitude to improve gra-
1200 dient quality, but this had little effect on the optimization (much overlap between same random
1201 seeds) (Fig. S6B). Finally, we increased n_{round} by an order of magnitude, which yielded conver-
1202 gence in one case, but no others. We found no way to improve the convergence rate of SNPE
1203 without making more aggressive hyperparameter choices requiring high numbers of simulations. In
1204 Figure 2C-D, we show samples from the random seed resulting in emergent property convergence
1205 at greatest entropy (EPI), the random seed resulting in greatest validation log probability (SNPE),
1206 and the result of all converged random seeds (SMC).

1207 5.3.5 Effect of RNN parameters on EPI and SNPE inferred distributions

1208 To clarify the difference in objectives of EPI and SNPE, we show their results on RNN models
1209 with different numbers of neurons N and random strength g . The parameters inferred by EPI
1210 consistently produces the same mean and variance of $\text{real}(\lambda_1)$ and λ_1^s , while those inferred by
1211 SNPE change according to the model definition (Fig. S7A). For $N = 2$ and $g = 0.01$, the SNPE
1212 posterior has greater concentration in eigenvalues around \mathbf{x}_0 than at $g = 0.1$, where the model has
1213 greater randomness (Fig. S7B top, orange). At both levels of g when $N = 2$, the posterior of SNPE
1214 has lower entropy than EPI at convergence (Fig. S7B top). However at $N = 10$, SNPE results in
1215 a predictive distribution of more widely dispersed eigenvalues (Fig. S7A bottom), and an inferred
1216 posterior with greater entropy than EPI (Fig. S7B bottom). We highlight these differences not
1217 to focus on an insightful trend, but to emphasize that these methods optimize different objectives

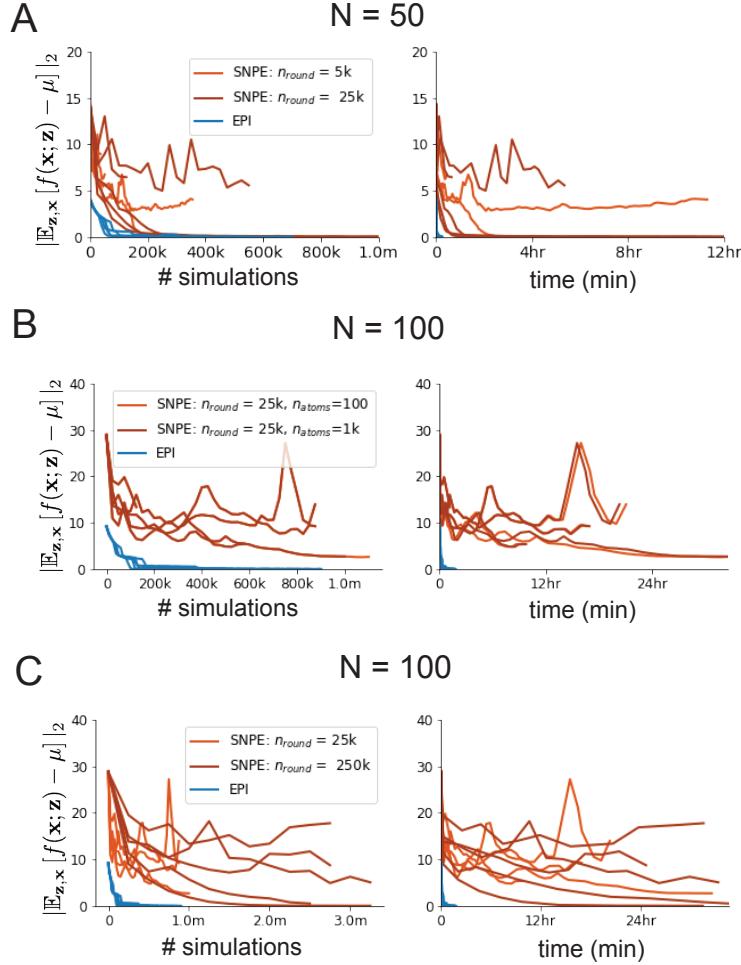


Figure S6: SNPE convergence was enabled by increasing n_{round} , not n_{atom} . **A.** Difference of mean predictions \mathbf{x}_0 throughout optimization at $N = 50$ with by simulation count (left) and wall time (right) of SNPE with $n_{\text{round}} = 5,000$ (light orange), SNPE with $n_{\text{round}} = 25,000$ (dark orange), and EPI (blue). Each line shows an individual random seed. **B.** Same conventions as A at $N = 100$ of SNPE with $n_{\text{atom}} = 100$ (light orange) and $n_{\text{atom}} = 1,000$ (dark orange). **C.** Same conventions as A at $N = 100$ of SNPE with $n_{\text{round}} = 25,000$ (light orange) and $n_{\text{round}} = 250,000$ (dark orange).

1218 with different implications.

1219 Note that SNPE converges when it's validation log probability has saturated after several rounds
1220 of optimization (Fig. S7C), and that EPI converges after several epochs of its own optimization
1221 to enforce the emergent property constraints (Fig. S7D blue). Importantly, as SNPE optimizes
1222 its posterior approximation, the predictive means change, and at convergence may be different
1223 than \mathbf{x}_0 (Fig. S7D orange, left). It is sensible to assume that predictions of a well-approximated
1224 SNPE posterior should closely reflect the data on average (especially given a uniform prior and
1225 a low degree of stochasticity), however this is not a given. Furthermore, no aspect of the SNPE
1226 optimization controls the variance of the predictions (Fig. S7D orange, right).

1227 5.4 Primary visual cortex

1228 5.4.1 V1 model

1229 E-I circuit models, rely on the assumption that inhibition can be studied as an indivisible unit,
1230 despite ample experimental evidence showing that inhibition is instead composed of distinct ele-
1231 ments [63]. In particular three types of genetically identified inhibitory cell-types – parvalbumin
1232 (P), somatostatin (S), VIP (V) – compose 80% of GABAergic interneurons in V1 [61–63], and follow
1233 specific connectivity patterns (Fig. 3A) [64], which lead to cell-type specific computations [47, 96].
1234 Currently, how the subdivision of inhibitory cell-types, shapes correlated variability by reconfigur-
1235 ing recurrent network dynamics is not understood.

1236 In the stochastic stabilized supralinear network [59], population rate responses \mathbf{x} to mean input \mathbf{h} ,
1237 recurrent input $W\mathbf{x}$ and slow noise ϵ are governed by

$$\tau \frac{d\mathbf{x}}{dt} = -\mathbf{x} + \phi(W\mathbf{x} + \mathbf{h} + \epsilon), \quad (68)$$

1238 where the noise is an Ornstein-Uhlenbeck process $\epsilon \sim OU(\tau_{noise}, \sigma)$

$$\tau_{noise} d\epsilon_\alpha = -\epsilon_\alpha dt + \sqrt{2\tau_{noise}} \tilde{\sigma}_\alpha dB \quad (69)$$

1239 with $\tau_{noise} = 5\text{ms} > \tau = 1\text{ms}$. The noisy process is parameterized as

$$\tilde{\sigma}_\alpha = \sigma_\alpha \sqrt{1 + \frac{\tau}{\tau_{noise}}}, \quad (70)$$

1240 so that σ parameterizes the variance of the noisy input in the absence of recurrent connectivity
1241 ($W = \mathbf{0}$). As contrast $c \in [0, 1]$ increases, input to the E- and P-populations increases relative to

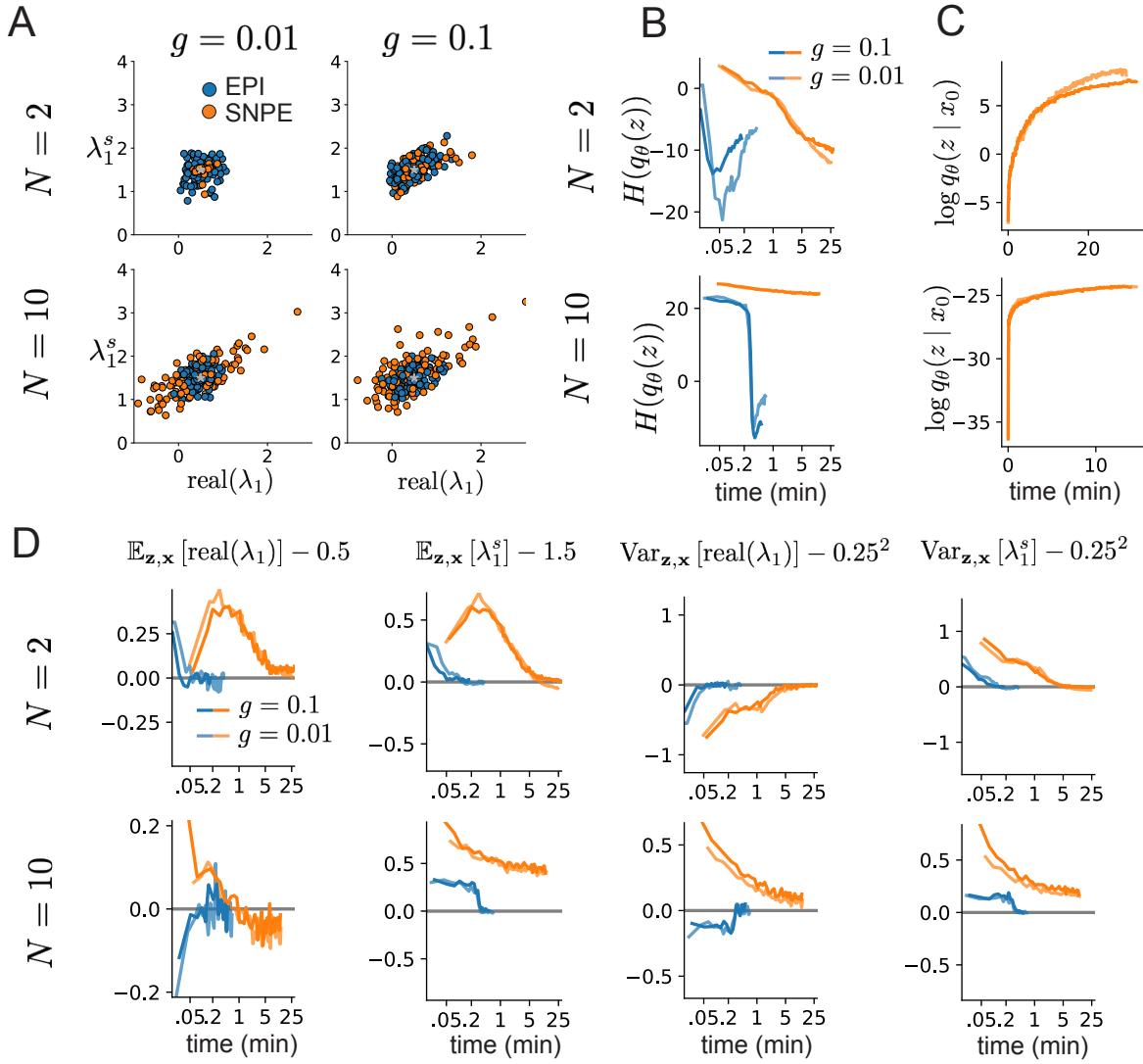


Figure S7: Model characteristics affect predictions of posteriors inferred by SNPE, while predictions of parameters inferred by EPI remain fixed. **A.** Predictive distribution of EPI (blue) and SNPE (orange) inferred connectivity of RNNs exhibiting stable amplification with $N = 2$ (top), $N = 10$ (bottom), $g = 0.01$ (left), and $g = 0.1$ (right). **B.** Entropy of parameter distribution approximations throughout optimization with $N = 2$ (top), $N = 10$ (bottom), $g = 0.1$ (dark shade), and $g = 0.01$ (light shade). **C.** Validation log probabilities throughout SNPE optimization. Same conventions as B. **D.** Adherence to EPI constraints. Same conventions as B.

¹²⁴² a baseline input $\mathbf{h} = \mathbf{h}_b + c\mathbf{h}_c$. Connectivity (W_{fit}) and input ($\mathbf{h}_{b,\text{fit}}$ and $\mathbf{h}_{c,\text{fit}}$) parameters were fit
¹²⁴³ using the deterministic V1 circuit model [47]

$$W_{\text{fit}} = \begin{bmatrix} W_{EE} & W_{EP} & W_{ES} & W_{EV} \\ W_{PE} & W_{PP} & W_{PS} & W_{PV} \\ W_{SE} & W_{SP} & W_{SS} & W_{SV} \\ W_{VE} & W_{VP} & W_{VS} & W_{VV} \end{bmatrix} = \begin{bmatrix} 2.18 & -1.19 & -.594 & -.229 \\ 1.66 & -.651 & -.680 & -.242 \\ .895 & -5.22 \times 10^{-3} & -1.51 \times 10^{-4} & -.761 \\ 3.34 & -2.31 & -.254 & -2.52 \times 10^{-4} \end{bmatrix}, \quad (71)$$

$$\mathbf{h}_{b,\text{fit}} = \begin{bmatrix} .416 \\ .429 \\ .491 \\ .486 \end{bmatrix}, \quad (72)$$

¹²⁴⁴ and

$$\mathbf{h}_{c,\text{fit}} = \begin{bmatrix} .359 \\ .403 \\ 0 \\ 0 \end{bmatrix}. \quad (73)$$

¹²⁴⁵ To obtain rates on a realistic scale (100-fold greater), we map these fitted parameters to an equiv-
¹²⁴⁶ alence class

$$W = \begin{bmatrix} W_{EE} & W_{EP} & W_{ES} & W_{EV} \\ W_{PE} & W_{PP} & W_{PS} & W_{PV} \\ W_{SE} & W_{SP} & W_{SS} & W_{SV} \\ W_{VE} & W_{VP} & W_{VS} & W_{VV} \end{bmatrix} = \begin{bmatrix} .218 & -.119 & -.0594 & -.0229 \\ .166 & -.0651 & -.068 & -.0242 \\ .0895 & -5.22 \times 10^{-4} & -1.51 \times 10^{-5} & -.0761 \\ .334 & -.231 & -.0254 & -2.52 \times 10^{-5} \end{bmatrix}, \quad (74)$$

$$\mathbf{h}_b = \begin{bmatrix} h_{b,E} \\ h_{b,P} \\ h_{b,S} \\ h_{b,V} \end{bmatrix} = \begin{bmatrix} 4.16 \\ 4.29 \\ 4.91 \\ 4.86 \end{bmatrix}, \quad (75)$$

1247 and

$$\mathbf{h}_c = \begin{bmatrix} h_{c,E} \\ h_{c,P} \\ h_{c,S} \\ h_{c,V} \end{bmatrix} = \begin{bmatrix} 3.59 \\ 4.03 \\ 0 \\ 0 \end{bmatrix}. \quad (76)$$

1248 Circuit responses are simulated using $T = 200$ time steps at $dt = 0.5\text{ms}$ from an initial condition
 1249 drawn from $\mathbf{x}(0) \sim U[10\text{Hz}, 25\text{Hz}]$. Standard deviation of the E-population $s_E(\mathbf{x}; \mathbf{z})$ is calculated
 1250 as the square root of the temporal variance from $t_{ss} = 75\text{ms}$ to $Tdt = 100\text{ms}$

$$s_E(\mathbf{x}; \mathbf{z}) = \sqrt{\mathbb{E}_{t > t_{ss}} [(x_E(t) - \mathbb{E}_{t > t_{ss}} [x_E(t)])^2]}. \quad (77)$$

1251 5.4.2 EPI details for the V1 model

1252 To write the emergent properties of Equation 7 in terms of the EPI optimization, we have

$$f(\mathbf{x}; \mathbf{z}) = s_E(\mathbf{x}; \mathbf{z}), \quad (78)$$

1253

$$\boldsymbol{\mu} = \begin{bmatrix} 5 \end{bmatrix} \quad (79)$$

1254 (or $\boldsymbol{\mu} = \begin{bmatrix} 10 \end{bmatrix}$), and

$$\boldsymbol{\sigma}^2 = \begin{bmatrix} 1^2 \end{bmatrix} \quad (80)$$

1255 (see Sections 5.1.3-5.1.4, and example in Section 5.1.5).

1256 For EPI in Figures 3D-E and S8, we used a real NVP architecture with three coupling layers
 1257 and two-layer neural networks of 50 units per layer. The normalizing flow architecture mapped
 1258 $z_0 \sim \mathcal{N}(\mathbf{0}, I)$ to a support of $\mathbf{z} = [\sigma_E, \sigma_P, \sigma_S, \sigma_V] \in [0.0, 0.5]^4$. EPI optimization was run using three
 1259 different random seeds for architecture initialization $\boldsymbol{\theta}$ with an augmented lagrangian coefficient of
 1260 $c_0 = 10^{-1}$, $\beta = 2$, a batch size $n = 100$, and simulated 100 trials to calculate average $s_E(\mathbf{x}; \mathbf{z})$ for
 1261 each $\mathbf{z}^{(i)}$. We used $i_{\max} = 2,000$ iterations per epoch. The distributions shown are those of the
 1262 architectures converging with criteria $N_{\text{test}} = 100$ at greatest entropy across three random seeds.
 1263 Optimization details are shown in Figure S9. The sums of squares of each pair of parameters are
 1264 shown for each EPI distribution in Figure S10. The plots are histograms of 500 samples from each
 1265 EPI distribution from which the significance p -values of Section 3.4 are determined.

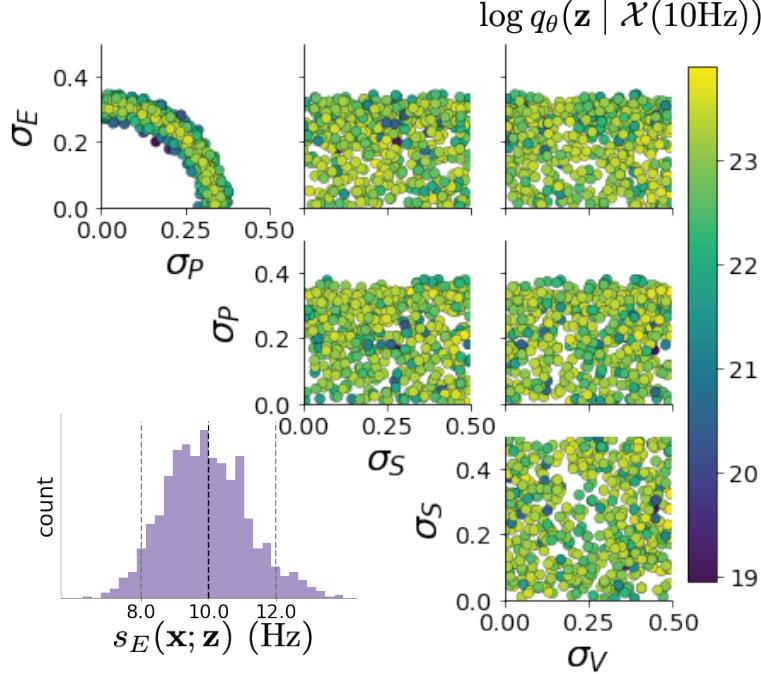


Figure S8: EPI inferred distribution for $\mathcal{X}(10\text{Hz})$.

1266 5.4.3 Sensitivity analyses

1267 In Fig. 3E, we visualize the modes of $q_\theta(\mathbf{z} \mid \mathcal{X})$ throughout the σ_E - σ_P marginal. At each local
1268 mode $\mathbf{z}^*(\sigma_P)$, where σ_P is fixed, we calculated the Hessian and visualized the sensitivity dimension
1269 in the direction of positive σ_E .

1270 5.4.4 Testing for the paradoxical effect

1271 The paradoxical effect occurs when a populations steady state rate is decreased (or increased)
1272 when an increase (decrease) in current is applied to that population [12]. To see which, if any,
1273 populations exhibited a paradoxical effect, we examined responses to changes in input (Fig. S11).
1274 Input magnitudes were chosen so that the effect is salient (0.002 for E and P, but 0.02 for S and
1275 V). Only the P-population exhibited the paradoxical effect at this connectivity W and input \mathbf{h} .

1276 5.4.5 Primary visual cortex: Mathematical intuition and challenges

1277 The dynamical system that we are working with can be written as

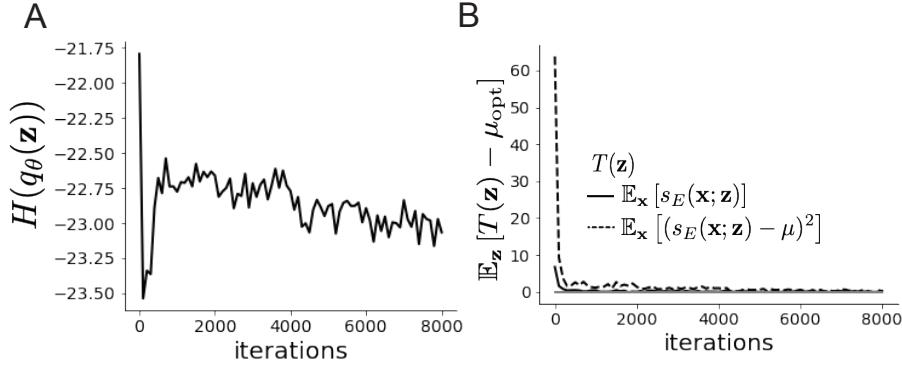


Figure S9: EPI optimization $q_\theta(\mathbf{z} \mid \mathcal{X}(5\text{Hz}))$ **A.** Entropy throughout optimization. **B.** The emergent property statistic means and variances converge to their constraints at 8,000 iterations following the fourth augmented lagrangian epoch.

$$\begin{aligned} dx &= \frac{1}{\tau}(-x + f(Wx + h + \epsilon))dt \\ d\epsilon &= -\frac{dt}{\tau_{\text{noise}}} \epsilon + \frac{\sqrt{2}}{\sqrt{\tau_{\text{noise}}}} \Sigma_\epsilon dW \end{aligned} \quad (81)$$

₁₂₇₈ Where in this paper we chose

$$\Sigma_\epsilon = \tau_{\text{noise}} \begin{bmatrix} \tilde{\sigma}_E & 0 & 0 & 0 \\ 0 & \tilde{\sigma}_P & 0 & 0 \\ 0 & 0 & \tilde{\sigma}_S & 0 \\ 0 & 0 & 0 & \tilde{\sigma}_V \end{bmatrix} \quad (82)$$

₁₂₇₉ where $\tilde{\sigma}_\alpha$ is the reparameterized standard deviation of the noise for population α from Equation
₁₂₈₀ 70.

₁₂₈₁ In order to compute this covariance, we define $v = \omega x + h + \epsilon$ and $S = I - \omega f'(v))$, to re-write Eq.
₁₂₈₂ (81) as an 8-dimensional system:

$$d \begin{pmatrix} \delta v \\ \epsilon \end{pmatrix} = - \begin{pmatrix} S & -\frac{\tau_{\text{noise}} - \tau}{\tau \tau_{\text{noise}}} I \\ 0 & \frac{1}{\tau_{\text{noise}}} I \end{pmatrix} \begin{pmatrix} \delta v \\ \epsilon \end{pmatrix} dt + \begin{pmatrix} 0 & \frac{\sqrt{2}}{\sqrt{\tau_{\text{noise}}}} \Sigma_\epsilon \\ 0 & \frac{\sqrt{2}}{\sqrt{\tau_{\text{noise}}}} \Sigma_\epsilon \end{pmatrix} d\mathbf{W} \quad (83)$$

₁₂₈₃ Where $d\mathbf{W}$ is a vector with the private noise of each variable. The $d\mathbf{W}$ term is multiplied by a
₁₂₈₄ non-diagonal matrix is because the noise that the voltage receives is the exact same than the one
₁₂₈₅ that comes from the OU process and not another process. The solution of this problem is given by
₁₂₈₆ the Lyapunov Equation [59, 66]:

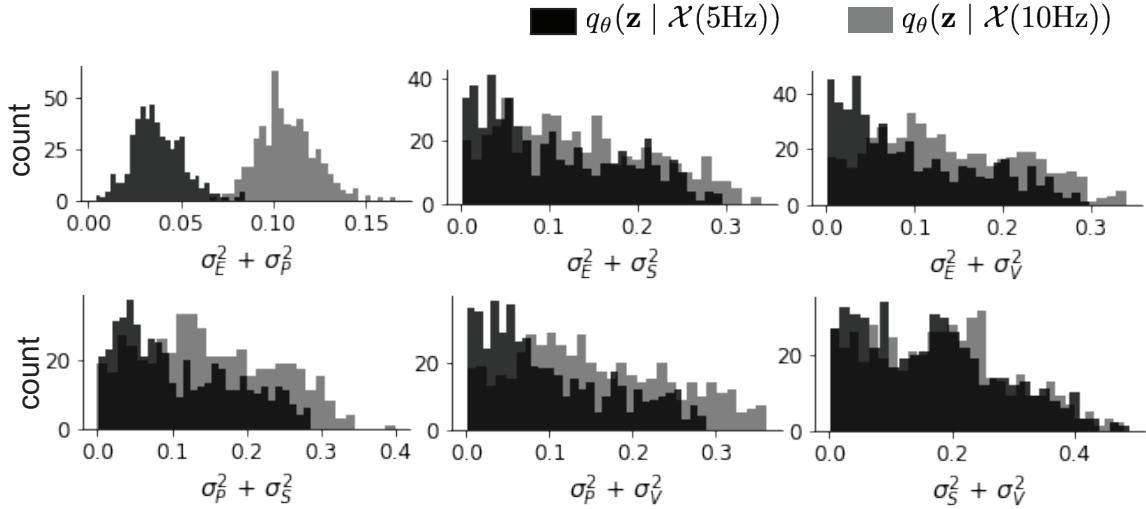


Figure S10: EPI predictive distributions of the sum of squares of each pair of noise parameters.

$$\begin{pmatrix} S & -\frac{\tau_{\text{noise}}-\tau}{\tau\tau_{\text{noise}}}I \\ 0 & \frac{1}{\tau_{\text{noise}}}I \end{pmatrix} \begin{pmatrix} \Lambda_v & \Lambda_c \\ \Lambda_c^T & \Lambda_\epsilon \end{pmatrix} + \begin{pmatrix} \Lambda_v & \Lambda_c \\ \Lambda_c^T & \Lambda_\epsilon \end{pmatrix} \begin{pmatrix} S^T & 0 \\ -\frac{\tau_{\text{noise}}-\tau}{\tau\tau_{\text{noise}}}I & \frac{1}{\tau_{\text{noise}}}I \end{pmatrix} = \begin{pmatrix} \frac{2}{\tau_{\text{noise}}}\Lambda_\epsilon & \frac{2}{\tau_{\text{noise}}}\Lambda_\epsilon \\ \frac{2}{\tau_{\text{noise}}}\Lambda_\epsilon & \frac{2}{\tau_{\text{noise}}}\Lambda_\epsilon \end{pmatrix} \quad (84)$$

¹²⁸⁷ To obtain an equation for Λ_v , we solve this block matrix multiplication:

$$S\Lambda_v + \Lambda_v S^T = \frac{2\Lambda_\epsilon}{\tau_{\text{noise}}} + \frac{\tau_{\text{noise}}^2 - \tau^2}{(\tau\tau_{\text{noise}})^2} \left(\left(\frac{1}{\tau_{\text{noise}}}I + S \right)^{-1} \Lambda_\epsilon + \Lambda_\epsilon \left(\frac{1}{\tau_{\text{noise}}}I + S^T \right)^{-1} \right) \quad (85)$$

Which is another Lyapunov Equation, now in 4 dimensions. In the simplest case in which $\tau_{\text{noise}} = \tau$, the voltage is directly driven by white noise, and Λ_v can be expressed in powers of S and S^T . Because S satisfies its own polynomial equation (Cayley Hamilton theorem), there will be 4 coefficients for the expansion of S and 4 for S^T , resulting in 16 coefficients that define Λ_v for a given S . Due to symmetry arguments [66], in this case the diagonal elements of the covariance matrix of the voltage will have the form:

$$\Lambda_{v_{ii}} = \sum_{i=\{E,P,S,V\}} g_i(S) \sigma_{ii}^2 \quad (86)$$

¹²⁸⁸ These coefficients $g_i(S)$ are complicated functions of the Jacobian of the system. Although expres-
¹²⁸⁹ sions for these coefficients can be found explicitly, only numerical evaluation of those expressions
¹²⁹⁰ determine which components of the noisy input are going to strongly influence the variability of ex-
¹²⁹¹ citatory population. Showing the generality of this dependence in more complicated noise scenarios
¹²⁹² (e.g. $\tau_{\text{noise}} > \tau$ as in Section 3.4), is the focus of current research.

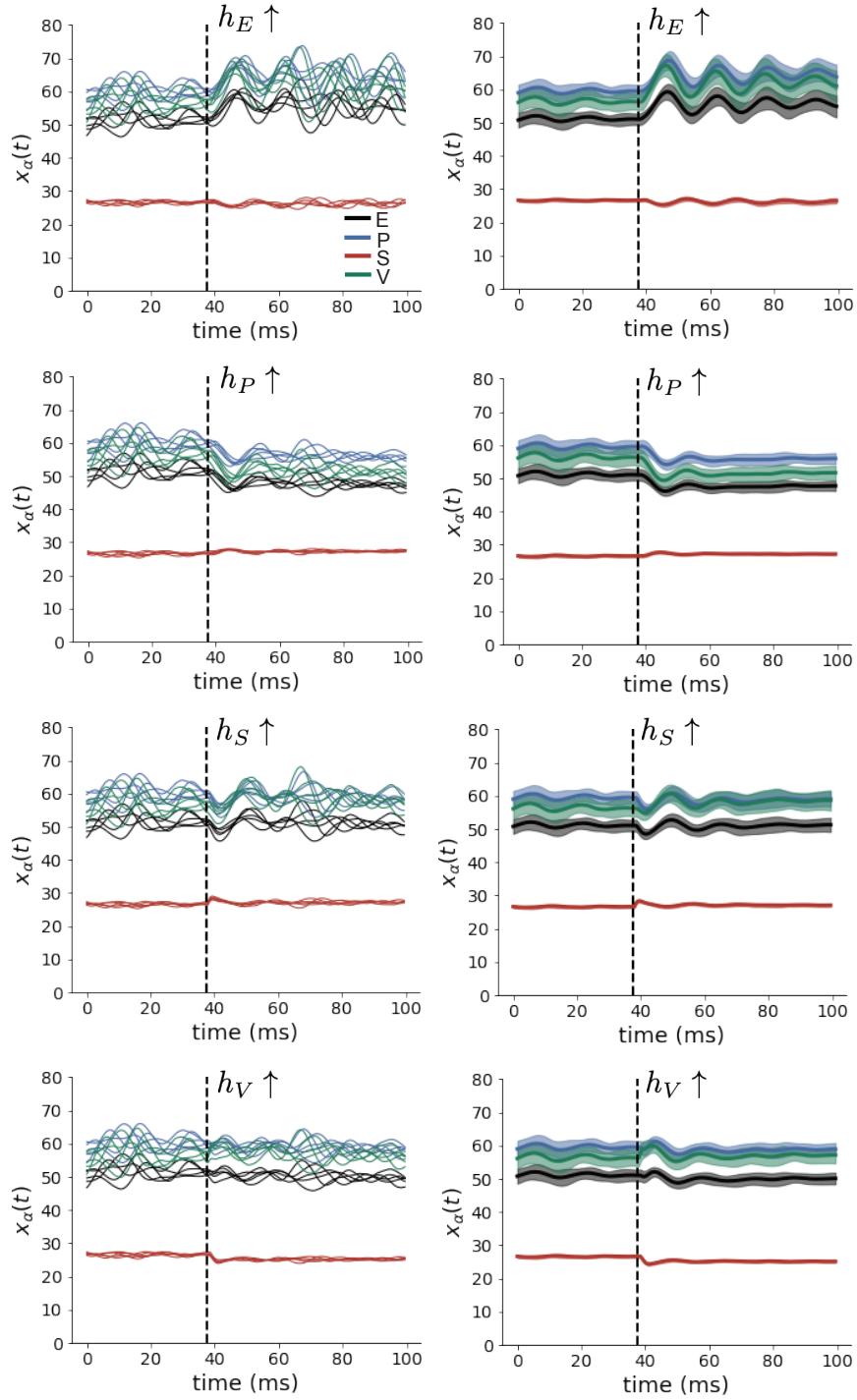


Figure S11: (Left) SSSN simulations for small increases in neuron-type population input. (Right) Average (solid) and standard deviation (shaded) of stochastic fluctuations of responses.

1293 **5.5 Superior colliculus**

1294 **5.5.1 SC model**

1295 The ability to switch between two separate tasks throughout randomly interleaved trials, or “rapid
 1296 task switching,” has been studied in rats, and midbrain superior colliculus (SC) has been shown to
 1297 play an important role in this computation [67]. Neural recordings in SC exhibited two populations of
 1298 neurons that simultaneously represented both task context (Pro or Anti) and motor response (con-
 1299 tralateral or ipsilateral to the recorded side), which led to the distinction of two functional classes:
 1300 the Pro/Contra and Anti/Ipsi neurons [48]. Given this evidence, Duan et al. proposed a model
 1301 with four functionally-defined neuron-type populations: two in each hemisphere corresponding to
 1302 the Pro/Contra and Anti/Ipsi populations. We study how the connectivity of this neural circuit
 1303 governs rapid task switching ability.

1304 The four populations of this model are denoted as left Pro (LP), left Anti (LA), right Pro (RP)
 1305 and right Anti (RA). Each unit has an activity (x_α) and internal variable (u_α) related by

$$x_\alpha = \phi(u_\alpha) = \left(\frac{1}{2} \tanh\left(\frac{u_\alpha - a}{b}\right) + \frac{1}{2} \right), \quad (87)$$

1306 where $\alpha \in \{LP, LA, RA, RP\}$, $a = 0.05$ and $b = 0.5$ control the position and shape of the nonlin-
 1307 earity. We order the neural populations of x and u in the following manner

$$\mathbf{x} = \begin{bmatrix} x_{LP} \\ x_{LA} \\ x_{RP} \\ x_{RA} \end{bmatrix} \quad \mathbf{u} = \begin{bmatrix} u_{LP} \\ u_{LA} \\ u_{RP} \\ u_{RA} \end{bmatrix}, \quad (88)$$

1308 which evolve according to

$$\tau \frac{d\mathbf{u}}{dt} = -\mathbf{u} + W\mathbf{x} + \mathbf{h} + d\mathbf{B}. \quad (89)$$

1309 with time constant $\tau = 0.09s$, step size 24ms and Gaussian noise $d\mathbf{B}$ of variance 0.2^2 . These
 1310 hyperparameter values are motivated by modeling choices and results from [48].

1311 The weight matrix has 4 parameters for self sW , vertical vW , horizontal hW , and diagonal dW
 1312 connections:

$$W = \begin{bmatrix} sW & vW & hW & dW \\ vW & sW & dW & hW \\ hW & dW & sW & vW \\ dW & hW & vW & sW \end{bmatrix}. \quad (90)$$

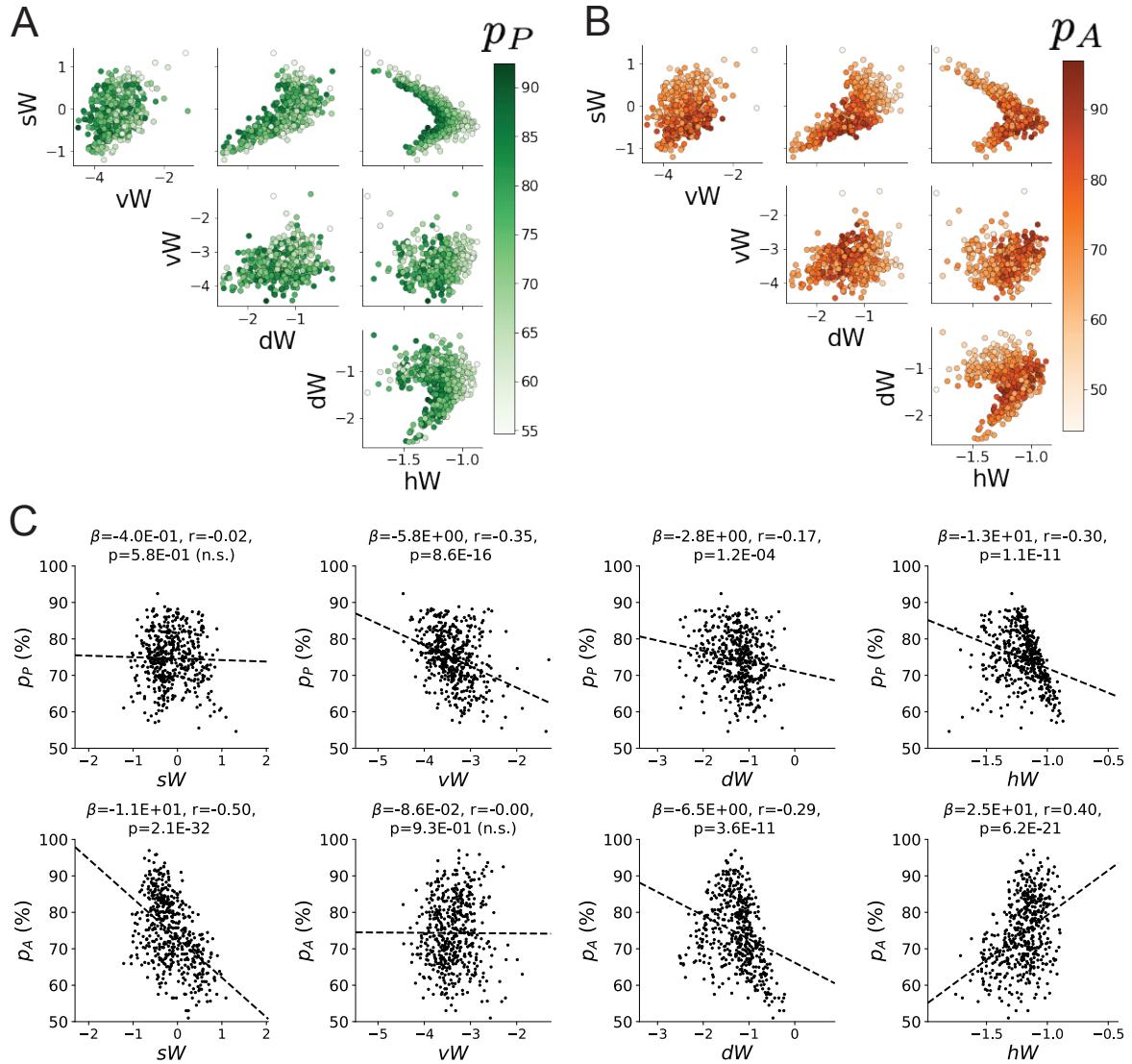


Figure S12: **A.** Same pairplot as Fig. 4C colored by Pro task accuracy. **B.** Same as A colored by Anti task accuracy. **C.** Connectivity parameters of EPI distributions versus task accuracies. β is slope coefficient of linear regression, r is correlation, and p is the two-tailed p-value.

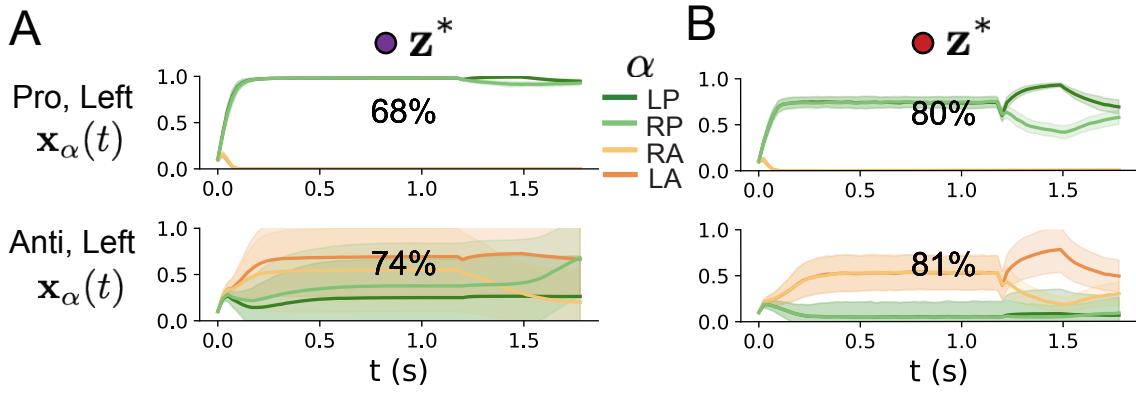


Figure S13: **A.** Simulations in network regime 1: $\mathbf{z}^*(sW = -0.75)$. **B.** Simulations in network regime 2: $\mathbf{z}^*(sW = 0.75)$.

₁₃₁₃ We study the role of parameters $\mathbf{z} = [sW, vW, hW, dW]^\top$ in rapid task switching.

₁₃₁₄ The circuit receives four different inputs throughout each trial, which has a total length of 1.8s.

$$\mathbf{h} = \mathbf{h}_{\text{constant}} + \mathbf{h}_{\text{P,bias}} + \mathbf{h}_{\text{rule}} + \mathbf{h}_{\text{choice-period}} + \mathbf{h}_{\text{light}}. \quad (91)$$

₁₃₁₅ There is a constant input to every population,

$$\mathbf{h}_{\text{constant}} = I_{\text{constant}}[1, 1, 1, 1]^\top, \quad (92)$$

₁₃₁₆ a bias to the Pro populations

$$\mathbf{h}_{\text{P,bias}} = I_{\text{P,bias}}[1, 0, 1, 0]^\top, \quad (93)$$

₁₃₁₇ rule-based input depending on the condition

$$\mathbf{h}_{\text{P,rule}}(t) = \begin{cases} I_{\text{P,rule}}[1, 0, 1, 0]^\top, & \text{if } t \leq 1.2s \\ 0, & \text{otherwise} \end{cases} \quad (94)$$

₁₃₁₈

$$\mathbf{h}_{\text{A,rule}}(t) = \begin{cases} I_{\text{A,rule}}[0, 1, 0, 1]^\top, & \text{if } t \leq 1.2s \\ 0, & \text{otherwise} \end{cases}, \quad (95)$$

₁₃₁₉ a choice-period input

$$\mathbf{h}_{\text{choice}}(t) = \begin{cases} I_{\text{choice}}[1, 1, 1, 1]^\top, & \text{if } t > 1.2s \\ 0, & \text{otherwise} \end{cases}, \quad (96)$$

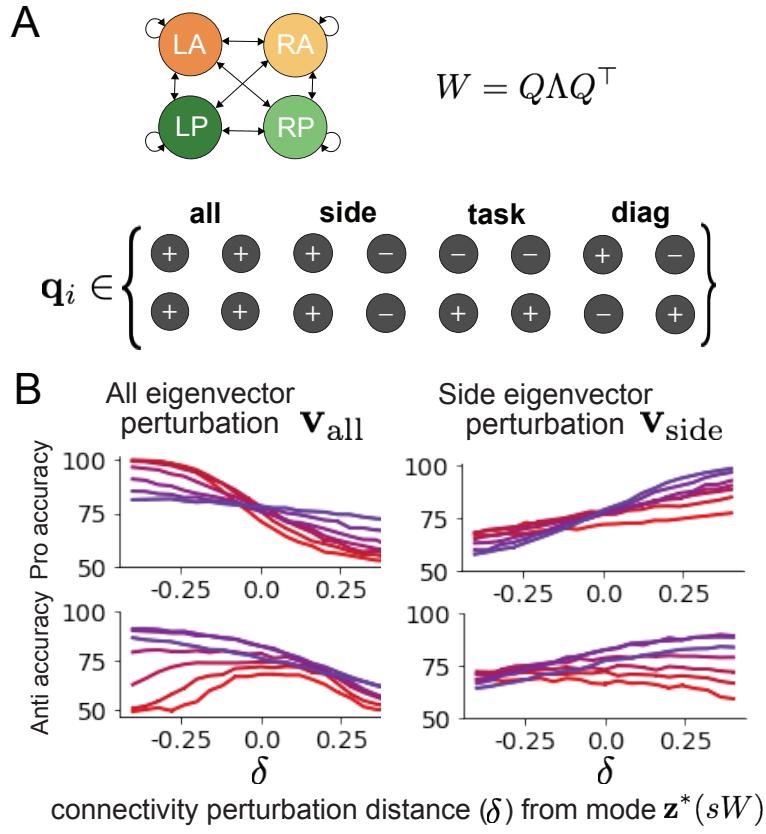


Figure S14: **A.** Invariant eigenvectors of connectivity matrix W . **B.** Accuracies for connectivity perturbations when changing λ_{all} and λ_{side} (λ_{task} and λ_{diag} shown in Fig. 4D).

1320 and an input to the right or left-side depending on where the light stimulus is delivered

$$\mathbf{h}_{\text{light}}(t) = \begin{cases} I_{\text{light}}[1, 1, 0, 0]^\top, & \text{if } 1.2s < t < 1.5s \text{ and Left} \\ I_{\text{light}}[0, 0, 1, 1]^\top, & \text{if } 1.2s < t < 1.5s \text{ and Right} \\ 0, & \text{otherwise} \end{cases} \quad (97)$$

1321 The input parameterization was fixed to $I_{\text{constant}} = 0.75$, $I_{\text{P,bias}} = 0.5$, $I_{\text{P,rule}} = 0.6$, $I_{\text{A,rule}} = 0.6$,

1322 $I_{\text{choice}} = 0.25$, and $I_{\text{light}} = 0.5$.

1323 5.5.2 Task accuracy calculation

1324 The accuracies of the Pro and Anti tasks are calculated as

$$p_P(\mathbf{x}; \mathbf{z}) = \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [d_P(\mathbf{x}; \mathbf{z})] \quad (98)$$

1325 and

$$p_A(\mathbf{x}; \mathbf{z}) = \mathbb{E}_{\mathbf{x} \sim p(\mathbf{x}|\mathbf{z})} [d_A(\mathbf{x}; \mathbf{z})] \quad (99)$$

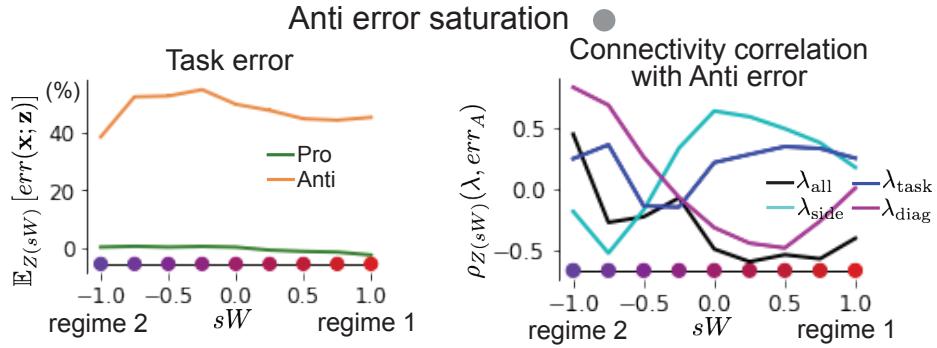


Figure S15: (Left) Mean and standard error of Pro and Anti error from regime 1 to regime 2 at $\gamma = 0.85$. (Right) Correlations of connectivity eigenvalues with Anti error from regime 1 to regime 2 at $\gamma = 0.85$.

1326 where $d_P(\mathbf{x}; \mathbf{z})$ and $d_A(\mathbf{x}; \mathbf{z})$ calculate the decision made in each trial (approximately 1 for correct
1327 and 0 for incorrect choices). Specifically,

$$d_P(\mathbf{x}; \mathbf{z}) = \Theta[x_{LP}(t = 1.8s) - x_{RP}(t = 1.8s)] \quad (100)$$

1328 in Pro trials where the stimulus is on the left side, and Θ approximates the Heaviside step function.

1329 Similarly,

$$d_A(\mathbf{x}; \mathbf{z}) = \Theta[x_{RP}(t = 1.8s) - x_{LP}(t = 1.8s)] \quad (101)$$

1330 in Anti trials where the stimulus was on the left side. Our accuracy calculation only considers one
1331 stimulus presentation (Left), since the model is left-right symmetric. The accuracy is averaged over
1332 200 independent trials, and the Heaviside step function is approximated as

$$\Theta(\mathbf{x}) = \text{sigmoid}(\beta_\Theta \mathbf{x}), \quad (102)$$

1333 where $\beta_\Theta = 100$.

1334 5.5.3 EPI details for the SC model

1335 To write the emergent properties of Equation 9 in terms of the EPI optimization, we have

$$f(\mathbf{x}; \mathbf{z}) = \begin{bmatrix} d_P(\mathbf{x}; \mathbf{z}) \\ d_A(\mathbf{x}; \mathbf{z}) \end{bmatrix} \quad (103)$$

1336

$$\boldsymbol{\mu} = \begin{bmatrix} .75 \\ .75 \end{bmatrix}, \quad (104)$$

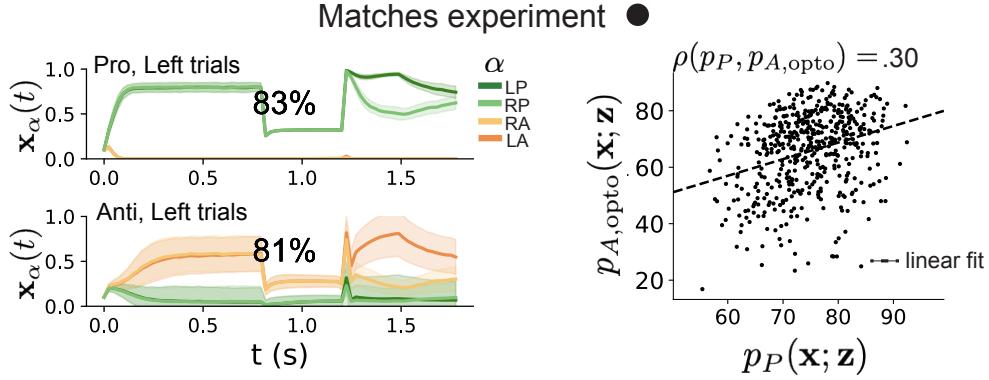


Figure S16: (Left) Mean and standard deviation (shading) of responses of the SC model at the mode of the EPI distribution to delay period inactivation at $\gamma = 0.675$. Accuracy in Pro (top) and Anti (bottom) task is shown as a percentage. (Right) Anti accuracy following delay period inactivation at $\gamma = 0.675$ versus accuracy in the Pro task across connectivities in the EPI distribution.

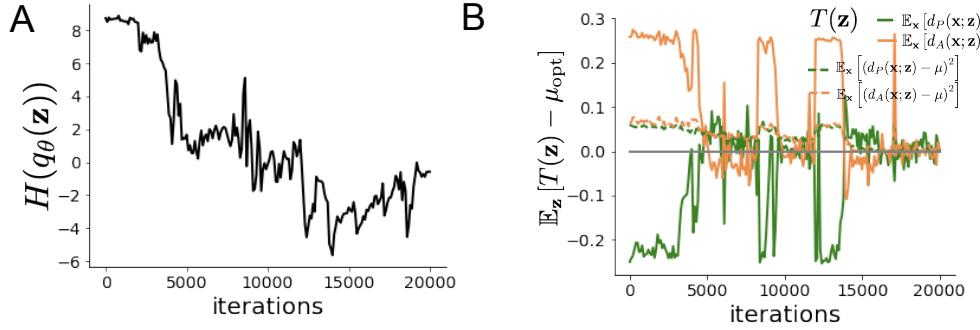


Figure S17: EPI optimization of the SC model producing rapid task switching. **A.** Entropy throughout optimization. **B.** The emergent property statistic means and variances converge to their constraints at 20,000 iterations following the tenth augmented lagrangian epoch.

¹³³⁷ and

$$\sigma^2 = \begin{bmatrix} .075^2 \\ .075^2 \end{bmatrix} \quad (105)$$

¹³³⁸ (see Sections 5.1.3-5.1.4, and example in Section 5.1.5).

¹³³⁹ Throughout optimization, the augmented lagrangian parameters η and c , were updated after each
¹³⁴⁰ epoch of $i_{\max} = 2,000$ iterations (see Section 5.1.4). The optimization converged after ten epochs
¹³⁴¹ (Fig. S16).

¹³⁴² For EPI in Fig. 4C, we used a real NVP architecture with three coupling layers of affine transfor-
¹³⁴³ mations parameterized by two-layer neural networks of 50 units per layer. The initial distribution
¹³⁴⁴ was a standard isotropic gaussian $\mathbf{z}_0 \sim \mathcal{N}(\mathbf{0}, I)$ mapped to a support of $\mathbf{z}_i \in [-5, 5]$. We used an

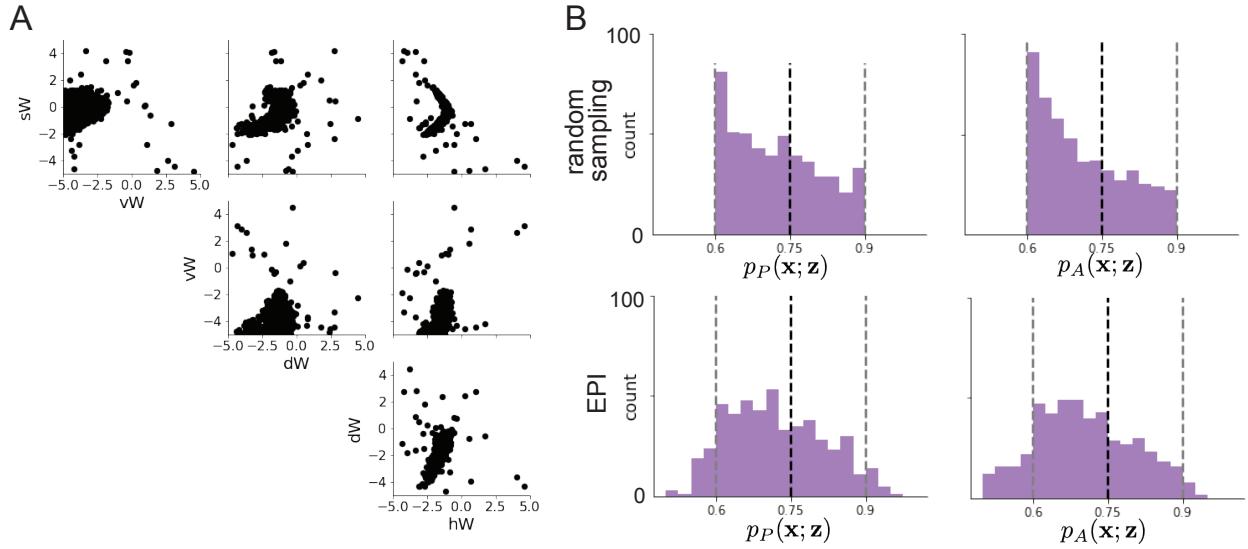


Figure S18: **A.** Rapid task switching SC connectivities obtained from random sampling. **B.** Task accuracies of the inferred distributions from random sampling (top) and EPI (bottom).

1345 augmented lagrangian coefficient of $c_0 = 10^2$, a batch size $n = 100$, and $\beta = 2$. The distribution
 1346 was the greatest EPI distribution to converge across 5 random seeds with criteria $N_{\text{test}} = 25$.
 1347 The bend in the EPI distribution is not a spurious result of the EPI optimization. The structure
 1348 discovered by EPI matches the shape of the set of points returned from brute-force random sampling
 1349 (Fig. S18A) These connectivities were sampled from a uniform distribution over the range of each
 1350 connectivity parameter, and all parameters producing accuracy in each task within the range of
 1351 60% to 90% were kept. This set of connectivities will not match the distribution of EPI exactly,
 1352 since it is not conditioned on the emergent property. For example the parameter set returned by
 1353 the brute-force search is biased towards lower accuracies (Fig. S18B).

1354 5.5.4 Mode identification with EPI

1355 We found one mode of the EPI distribution for fixed values of sW from 1 to -1 in steps of 0.25.
 1356 To begin, we chose an initial parameter value from 500 parameter samples $\mathbf{z} \sim q_{\theta}(\mathbf{z} \mid \mathcal{X})$ that
 1357 had closest sW value to 1. We then optimized this estimate of the mode (for fixed sW) using
 1358 probability gradients of the deep probability distribution for 500 steps of gradient ascent with a
 1359 learning rate of 5×10^{-3} . The next mode (at $sW = 0.75$) was found using the previous mode as
 1360 the initialization. This and all subsequent optimizations used 200 steps of gradient ascent with a
 1361 learning rate of 1×10^{-3} , except at $sW = -1$ where a learning rate of 5×10^{-4} was used. During all

1362 mode identification optimizations, the learning rate was reduced by half (decay = 0.5) after every
1363 100 iterations.

1364 **5.5.5 Sample grouping by mode**

1365 For the analyses in Figure 5C and Figure S15, we obtained parameters for each step along the
1366 continuum between regimes 1 and 2 by sampling from the EPI distribution. Each sample was
1367 assigned to the closest mode $\mathbf{z}^*(sW)$. Sampling continued until 500 samples were assigned to each
1368 mode, which took 2.67 seconds (5.34ms/sample-per-mode). It took 9.59 minutes to obtain just
1369 5 samples for each mode with brute force sampling requiring accuracies between 60% and 90%
1370 in each task (115s/sample-per-mode). This corresponds to a sampling speed increase of roughly
1371 21,500 once the EPI distribution has been learned.

1372 **5.5.6 Sensitivity analysis**

1373 At each mode, we measure the sensitivity dimension (that of most negative eigenvalue in the Hessian
1374 of the EPI distribution) $\mathbf{v}_1(\mathbf{z}^*)$. To resolve sign degeneracy in eigenvectors, we chose $\mathbf{v}_1(\mathbf{z}^*)$ to have
1375 negative element in hW . This tells us what parameter combination rapid task switching is most
1376 sensitive to at this parameter choice in the regime.

1377 **5.5.7 Connectivity eigendecomposition and processing modes**

1378 To understand the connectivity mechanisms governing task accuracy, we took the eigendecomposi-
1379 tion of the connectivity matrices $W = Q\Lambda Q^{-1}$, which results in the same eigenmodes \mathbf{q}_i for all W
1380 parameterized by \mathbf{z} (Fig. S14A). These eigenvectors are always the same, because the connectivity
1381 matrix is symmetric and the model also assumes symmetry across hemispheres, but the eigenvalues
1382 of connectivity (or degree of eigenmode amplification) change with \mathbf{z} . These basis vectors have in-
1383 tuitive roles in processing for this task, and are accordingly named the *all* eigenmode - all neurons
1384 co-fluctuate, *side* eigenmode - one side dominates the other, *task* eigenmode - the Pro or Anti pop-
1385 ulations dominate the other, and *diag* mode - Pro- and Anti-populations of opposite hemispheres
1386 dominate the opposite pair. Due to the parametric structure of the connectivity matrix, the pa-
1387 rameters \mathbf{z} are a linear function of the eigenvalues $\boldsymbol{\lambda} = [\lambda_{\text{all}}, \lambda_{\text{side}}, \lambda_{\text{task}}, \lambda_{\text{diag}}]^\top$ associated with these
1388 eigenmodes.

$$\mathbf{z} = A\boldsymbol{\lambda} \quad (106)$$

$$A = \frac{1}{4} \begin{bmatrix} 1 & 1 & 1 & 1 \\ 1 & -1 & -1 & 1 \\ 1 & 1 & -1 & -1 \\ 1 & -1 & 1 & -1 \end{bmatrix}. \quad (107)$$

1390 We are interested in the effect of raising or lowering the amplification of each eigenmode in the
 1391 connectivity matrix by perturbing individual eigenvalues λ . To test this, we calculate the unit
 1392 vector of changes in the connectivity \mathbf{z} that result from a change in the associated eigenvalues

$$\mathbf{v}_a = \frac{\frac{\partial \mathbf{z}}{\partial \lambda_a}}{\left\| \frac{\partial \mathbf{z}}{\partial \lambda_a} \right\|_2}, \quad (108)$$

1393 where

$$\frac{\partial \mathbf{z}}{\partial \lambda_a} = A \mathbf{e}_a, \quad (109)$$

1394 and e.g. $\mathbf{e}_{\text{all}} = [1, 0, 0, 0]^\top$. So \mathbf{v}_a is the normalized column of A corresponding to eigenmode
 1395 a . The parameter dimension \mathbf{v}_a ($a \in \{\text{all, side, task, and diag}\}$) that increases the eigenvalue of
 1396 connectivity λ_a is \mathbf{z} -invariant (Equation 109) and $\mathbf{v}_a \perp \mathbf{v}_{b \neq a}$. By perturbing \mathbf{z} along \mathbf{v}_a , we
 1397 can examine how model function changes by directly modulating the connectivity amplification of
 1398 specific eigenmodes, which having interpretable roles in processing in each task.

1399 5.5.8 Modeling optogenetic silencing.

1400 We tested whether the inferred SC model connectivities could reproduce experimental effects of
 1401 optogenetic inactivation in rats [48]. During periods of simulated optogenetic inactivation, activity
 1402 was decreased proportional to the optogenetic strength $\gamma \in [0, 1]$

$$x_\alpha = (1 - \gamma)\phi(u_\alpha). \quad (110)$$

1403 Delay period inactivation was from $0.8 < t < 1.2$.