Network inference in the nonequilibrium steady state

Simon L. Dettmer,1,* H. Chau Nguyen,2‡ and Johannes Berg1,†

1Institute for Theoretical Physics, University of Cologne, Zülpicher Straße 77, 50937 Cologne, Germany
2Max-Planck-Institut für Physik komplexer Systeme, Nöthnitzer Str. 38, 01187 Dresden, Germany

(Received 25 July 2016; published 10 November 2016)

Nonequilibrium systems lack an explicit characterization of their steady state like the Boltzmann distribution for equilibrium systems. This has drastic consequences for the inference of the parameters of a model when its dynamics lacks detailed balance. Such nonequilibrium systems occur naturally in applications like neural networks and gene regulatory networks. Here, we focus on the paradigmatic asymmetric Ising model and show that we can learn its parameters from independent samples of the nonequilibrium steady state. We present both an exact inference algorithm and a computationally more efficient, approximate algorithm for weak interactions based on a systematic expansion around mean-field theory. Obtaining expressions for magnetizations and two- and three-point spin correlations, we establish that these observables are sufficient to infer the model parameters. Further, we discuss the symmetries characterizing the different orders of the expansion around the mean field and show how different types of dynamics can be distinguished on the basis of samples from the nonequilibrium steady state.

DOI: 10.1103/PhysRevE.94.052116

I. INTRODUCTION

Inverse problems in statistical physics are motivated by the challenges of big data in different fields, especially high-throughput experiments in biology: Can one learn, for instance, the synaptic connections between neurons from observations of neural activity [1] or the regulatory interactions between genes from gene expression levels [2]? Inverse statistical problems such as these also include the determination of three-dimensional protein structures [3], the inference of fitness landscapes [4], and flocking dynamics [5]. The paradigmatic inverse statistical problem is the inverse Ising problem, which seeks to infer the parameters of a spin model—external fields and interactions between spins—from observables like magnetizations and spin correlations. For the equilibrium case, which is characterized by symmetric interactions between pairs of spins and detailed balance, a wide range of approaches has been developed on the basis of the Boltzmann distribution [6]. Yet in many applications, like neural networks and gene regulatory networks, interactions are generally asymmetric. For instance, a synaptic connection from neuron A to neuron B does not imply a reverse connection back from B to A. The resulting nonequilibrium steady state (NESS) lacks detailed balance and is not described by a Boltzmann distribution. We ask if it is possible to learn the parameters of a nonequilibrium model from independent samples of the NESS, even though the probability with which each state of the system occurs in the long-time limit is unknown. The key result of this paper is the identification of observables from which the parameters of a nonequilibrium model can be reconstructed and a systematic procedure to infer the model parameters based on these observables.

II. THE ASYMMETRIC ISING MODEL

For concreteness, we start with the asymmetric Ising model in discrete time under so-called Glauber dynamics [7]: At a given time $t$, the state of a system of $N$ binary spins is characterized by variables $s_i(t)$ with $i=1,\ldots,N$. The dynamics of spins is defined by randomly picking a spin variable, say $i$, at each time step. The value of that spin variable is then updated, with $s_i(t+1) = \pm 1$ sampled from the probability distribution

$$w(s_i(t+1)|s(t)) = \frac{\exp[s_i(t+1)\theta_i(t)]}{2\cosh(\theta_i(t))}, \quad (1)$$

where the effective local field is

$$\theta_i(t) = h_i + \sum_{j=1}^{N} J_{ij}s_j(t), \quad (2)$$

with external fields $h_i$ and couplings between spins $J_{ij}$. This dynamics has been used as a model of neural dynamics [8] and as a model of gene expression dynamics [9]. Similar to this sequential dynamics, which updates one spin after the other, one can define a dynamics with parallel updates, where the updates, (1), are carried out simultaneously for all spins.

For a symmetric coupling matrix without self-couplings, the Glauber dynamics (1), converges to the equilibrium state characterized by the Boltzmann distribution $p_B(s) = e^{-\mathcal{H}(s)}/Z$ with the well-known Ising Hamiltonian

$$\mathcal{H}(s) = -\sum_i s_i(h_i + \sum_{j=1}^{N} J_{ij}s_j). \quad (3)$$

(Fort convenience we have subsumed the inverse temperature into the couplings and fields.) For asymmetric couplings, however, Glauber dynamics (1), converges to a nonequilibrium steady state, which lacks detailed balance and is hard to characterize. In the inverse problem, the task is to infer the parameters of the asymmetric Ising model, namely, the couplings $J_{ij}$ and external fields $h_i$ of (2). This is a comparatively easy task when we can observe time series of consecutive states of the system $s(t),s(t+1),s(t+2),\ldots$. Using the dynamical rule, (1), the probability of a particular trajectory $\prod_t w(s(t+1)|s(t))$ can be
written down explicitly and be maximized with respect to the
couplings and fields [10,11] in polynomial time in \( N \) and the
length of the trajectory. This yields the maximum likelihood
estimate of the model parameters. An estimate of the couplings
and fields that can be computed even more rapidly has been
derived using mean-field theory [10,12].

However, there are situations where a time series of the
system’s dynamics is not available. An example is genomewide
gene expression levels measured in single cells, a process
which involves the physical destruction of cells. In such cases,
only independent samples from the nonequilibrium steady
state are available. Beyond the practical relevance, it is also a
fundamental question whether we can characterize the NESS
sufficiently well to solve the inverse problem.

Already elementary arguments show that, unlike in the
equilibrium case [6,13], pairwise spin correlations are insuf-
sicient to infer the model parameters: the matrix of pairwise
interactions \([6,13]\), pairwise spin correlations are insuf-
sufficiently well to solve the inverse problem.

Beyond the practical relevance, it is also a
fundamental question whether we can characterize the NESS
sufficiently well to solve the inverse problem.

In the following, we write the magnetizations and
points correlations self-consistently as single-time expecta-
tions in the steady state involving the effective local fields, (2).
Further, we employ an expansion around a probability distri-
bution factorizing in the spins (mean-field theory) to derive
magnetizations and two- and three-point correlations as an
explicit function of the couplings and external fields. By inverting
either of these relationships we can solve the inverse problem.

We consider the magnetizations \( m_i \equiv \langle s_i \rangle \) in the steady
state and the fluctuations \( \delta s_i \equiv (s_i - m_i) \) of spins around
this mean. By averaging over the statistics, (1), we obtain for the
magnetizations and the \( n \)-point connected correlations
\( C_{i_1, i_2, \ldots, i_n} \equiv \langle \delta s_{i_1} \delta s_{i_2} \ldots \delta s_{i_n} \rangle \)

\[
m_i = \langle \tanh(\theta_i) \rangle = \sum_s p(s|\mathbf{h}, \mathbf{J}) \tanh(\theta_i(s|\mathbf{h}, \mathbf{J})) , \tag{3}
\]

\[
C_{i_1, \ldots, i_n} = \frac{1}{n} \sum_{k=1}^{n} \left( \prod_{j=1}^{n} \delta s_{i_j} \right) \left[ \tanh(\theta_{i_k}) - m_{i_k} \right] , \tag{4}
\]

where \( \{i_1, \ldots, i_n\} \subset \{1, \ldots, N\} \) is a subset of \( n \) spins and
\( p(s|\mathbf{h}, \mathbf{J}) \) denotes the steady-state probability over spin con-
figurations \( s \). These equations are a set of self-consistent
equations whose left-hand side gives magnetizations and
correlations, which together specify the probability distribution
\( p(s|\mathbf{h}, \mathbf{J}) \) in the NESS. The right-hand sides depend
on this distribution via averages over functions of \( \theta_i = h_i + \sum_{j=1}^{N} J_{ij}s_j \). A similar result holds for a dynamics with parallel
updates, where all spins are updated simultaneously and inde-
dependently during each time step under the stochastic update
rule

\[
\omega(s(t + 1)|s(t)) = \prod_{i=1}^{N} \frac{\exp[s_i(t + 1)\theta_i(t)]}{2\cosh(\theta_i(t))} , \tag{5}
\]

For parallel updates the magnetizations are unchanged from the sequential case but for the correlations one finds

\[
C_{i_1, \ldots, i_n}^{\text{par}} = \left( \prod_{l=1}^{n} \left[ \tanh(\theta_{i_l}) - m_{i_l} \right] \right) . \tag{6}
\]

Given independent samples from the steady state, the ex-
pectations in (3) and (4) can be evaluated numerically by averaging over the sampled configurations [for parallel updates we evaluate (3) and (6)].

IV. AN EXPANSION AROUND MEAN-FIELD THEORY

Although the steady-state probability distribution \( p(s|\mathbf{h}, \mathbf{J}) \)
underlying the expectations is not known, it turns out that its moments can be calculated in a systematic ex-
pansion around a distribution factorizing in the spins, \( q(s|h_q) \equiv p(s|h_q, J_q = 0) \). In equilibrium statistical physics,
this distribution is the well-known mean-field ansatz. Its application to the nonequilibrium setting was pioneered by
Kappen and Spanjers [14]. As usual in mean-field theory, the external fields \( \mathbf{h}_q = \mathbf{h}_q(\mathbf{J}) := \mathbf{h} - \lambda \mathbf{h} \) characterizing the
mean-field distribution \( q(s|h_q) \) are fixed by a self-consistent
equation for the magnetizations \( m(h_q, J_q = 0) = m(h, \mathbf{J}) \), so
the mean-field distribution yields the same magnetizations as
the original model with couplings \( \mathbf{J} \) and fields \( \mathbf{h} \). Considering
external fields \( \mathbf{h}_q + \lambda \delta h \) and couplings \( \lambda \mathbf{J} \), one can smoothly interpolate between \( \lambda = 0 \), describing the factorizing distri-
bution \( q \), to the NESS described by \( \lambda = 1 \). Expanding the
moments of this distribution in a Taylor-series around the
mean-field distribution \( \lambda = 0 \) gives

\[
m(h, \mathbf{J}) = \sum_{k=0}^{\infty} \frac{1}{k!} \frac{d^k m(h_q + \lambda \delta h, \lambda \mathbf{J})}{d\lambda^k} \bigg|_{\lambda=0} , \tag{7}
\]

Using this approach, Kappen and Spanjers computed the magnetizations and two-point correlations to second order in
\( \lambda \), [14],

\[
m_i = \tanh \left( h_i + \sum_{j=1}^{N} J_{ij} m_j - m_i \sum_{j=1}^{N} J_{ij}^2 (1-m_j^2) \right) . \tag{8}
\]
\[ C_{ij} = (1 - m_i^2)(1 - m_j^2) \left( J_{ij}^{\text{sym}} + m_i m_j (J_i^2 + J_j^2) \right) + \frac{1}{2} \sum_{k=1, k \neq i}^N J_{jk} J_{ik}^{\text{sym}} + J_{ik} J_{jk}^{\text{sym}} (1 - m_i^2) \right) , \tag{9} \]

where \( J^{\text{sym}} = \frac{1}{2}(J + J^T) \) and \( J^{\text{asym}} = \frac{1}{2}(J - J^T) \) are the symmetric and antisymmetric parts of the coupling matrix, respectively. Surprisingly, the magnetizations, \( \mathbf{m} \), computed to second order in \( \lambda \) agree with the TAP equation for the equilibrium magnetizations of a spin glass [15]. This agreement appears to be a coincidence; our result for the equilibrium magnetizations of a spin glass [15].

The symmetric part of the couplings \( J^{\text{sym}} = (J + J^T)/2 \) (a, c) generally has a lower reconstruction error than the antisymmetric part \( J^{\text{asym}} = (J - J^T)/2 \) (b, d).

\[ A_{ijk}(\mathbf{J}, \mathbf{m}) = J_{ij} J_{jk} m_j + J_{ji} J_{ki} m_i + J_{ik} J_{jk} m_i \tag{10} \]

This three-point correlations exhibit particular symmetries, which affect the reconstruction of model parameters. Already the two-point correlations, (9), depend, to first order in \( \lambda \), only on the symmetric part of the coupling matrix. However, also the three-point show symmetry; (10) is unchanged when the coupling matrix is replaced with its transpose so \( J^{\text{asym}} \) transforms to \( -J^{\text{asym}} \), since \( A_{ijk}(\mathbf{J}, \mathbf{m}) \) is quadratic in the couplings. Thus jointly solving (9) and (10) for the coupling matrix \( \mathbf{J} \) yields either the reconstruction of the original coupling matrix or its transpose. This binary symmetry is lifted only at third order in \( \lambda \) [see Eq. (A9) in Appendix A]. Therefore, the third-order terms give not only a quantitative improvement on the second order but are in fact necessary for successful inference.

V. PARAMETER INFERENCE

Given empirical samples from the NESS we can now solve the inverse problem in two ways. (i) In exact inference we jointly solve the self-consistent equations (3) and (4), up to three-point correlations for the couplings \( \mathbf{J} \) and external fields \( \mathbf{h} \). (ii) In mean-field inference we jointly solve the explicit correlation expressions (9) and (10) (taken to third order in \( \lambda \)), for the coupling matrix \( \mathbf{J} \). Subsequently solving the magnetization equations (8), for \( \mathbf{h} \) completes the parameter reconstruction.

To test these inference schemes, we numerically simulate a system of \( N = 10 \) spins with random asymmetric couplings. Off-diagonal entries in the matrix of couplings are chosen independently from a Gaussian distribution with zero mean and standard deviation \( \sqrt{N} \) (self-interactions are excluded: \( J_{ii} \equiv 0 \)), and external fields from a Gaussian distribution with zero mean and standard deviation \( \beta \). Samples of the state of the system under the Glauber dynamics, (1), with sequential updates are recorded at each update after an initial settling-in period of \( 10^5 \) updates to reach the steady state. Based on these measurements, we reconstruct the parameters by minimizing the sum of the relative squared prediction errors of the magnetization and two- and three-point correlation equations using the Levenberg-Marquardt algorithm (see Appendix B for details).

Figure 1 shows the reconstruction of the couplings for different numbers of samples and coupling strengths. Three-point correlations are small, and as a result, the inference is affected by sampling noise. For the exact inference, the reconstruction improves significantly with the number of samples (left-hand plots). For the mean-field inference, the correlations, (9) and (10), computed to finite order in \( \lambda \) become inaccurate in the limit of strong couplings, which can also limit the reconstruction quality. As a result, the mean-field reconstruction performs best for intermediate coupling strengths (right-hand plots). Also, the reconstruction error for the symmetric part of the couplings \( J^{\text{sym}} \) is smaller than that for the antisymmetric part \( J^{\text{asym}} \), since the former is primarily determined by the connected two-point correlations, (9), which are considerably larger than the three-point correlations. For this reason, fewer samples are required for the accurate inference of the symmetric part of the couplings. The reconstruction

FIG. 1. Couplings inferred from the NESS. We consider a system of \( N = 10 \) spins with random asymmetric couplings under the Glauber dynamics, (1); see the text. We plot the relative root-mean-squared reconstruction error \( \epsilon \) between the inferred and the true couplings versus the coupling strength \( \beta \) for different numbers of samples \( M \). Reconstruction errors (a, b) for the exact inference and (c, d) for the mean-field inference. The symmetric part of the couplings \( J^{\text{sym}} = (J + J^T)/2 \) (a, c) generally has a lower reconstruction error than the antisymmetric part \( J^{\text{asym}} = (J - J^T)/2 \) (b, d).
FIG. 2. External fields inferred from the NESS. We consider a system of \( N = 10 \) spins with random asymmetric couplings under Glauber dynamics, (1); see the text. We plot the relative root-mean-squared reconstruction error \( \epsilon \) between the inferred and the true external fields versus the coupling and external field strength \( \beta \) for the exact inference (a) and the mean-field inference (b).

of the external fields exhibits a similar behavior, although with much lower errors, and is shown in Fig. 2.

VI. MODEL SELECTION

Beyond estimating the parameters of a particular dynamical model, an important question is what type of dynamics produces a particular NESS. In inference, this question is known as the model selection problem. Here, we compare three dynamics: (i) Glauber dynamics with sequential updates,

(ii) Glauber dynamics with parallel updates, and (iii) equilibrium dynamics (sequential updates with \( J^{\text{asy}} = 0 \)). We start by taking independent samples from the NESS produced by a model with sequential dynamics as described above and calculate magnetizations and correlations. Next, we solve the exact self-consistent equations for the magnetizations and two- and three-point correlations for the different dynamics by minimizing the relative prediction error as above. This gives the model parameters for a particular dynamics that best reproduce the sampled correlations. In Fig. 3 we compare the three-point correlations predicted by these best fits of the three dynamical models with the sampled correlations. Indeed, the sequential model shows the best match with the sampled data, leading to the conclusion that of the three alternatives, the data were indeed most likely produced by a model with sequential Glauber dynamics. We find analogous results for samples generated by parallel updates, (5) (see Fig. 4).

This shows that one can distinguish the different types of dynamics based on samples from their NESS alone.

VII. THE INVERSE LANGEVIN PROBLEM

Our approach is not limited to the asymmetric Ising problem, its binary spins and discrete-time dynamics. Consider the dynamics of continuous variables \( x_i \) under a model of the form

\[
\dot{x}_i = f(\theta_i) - x_i + \xi_i(t),
\]
where the effective local field \( \theta_i(t) = h_i + \sum_j J_{ij} x_j(t) \), \( f(\theta) \) is an arbitrary monotonic function, and \( \xi_i(t) \) describes \( \delta \)-correlated white noise. This is a multivariate Langevin equation; the steady state, if it exists, generally does not obey detailed balance. For the particular choice \( f(\theta) = \tanh(\theta) \), this Langevin equation has magnetizations and correlations given by (3) and (4), and these results can be generalized easily to arbitrary choices of \( f(\theta) \). Hence these equations and their generalizations can also be used to solve the inverse problem for the class of nonequilibrium stochastic differential equations of the form of (12).

VIII. CONCLUSIONS

To conclude, we have used a self-consistent characterization of the nonequilibrium steady state for the inference of model parameters from independent samples, that is, without direct recourse to the dynamics of the system. We have shown that, in the case of the asymmetric Ising model, correlations beyond the two-point correlation are necessary for parameter inference and that three-point correlations are in fact sufficient for this task. However, there may be observables that are better suited for the inference of the asymmetric Ising model than three-point correlations. While there is no part of our reconstruction method which cannot be scaled up to larger system sizes (due to algorithmic constraints, for instance), a very large number of samples is required for reconstruction. There may be observables which remove this bottleneck and allow inference already with a smaller number of samples from the NESS.

APPENDIX A: MEAN-FIELD EQUATIONS TO THIRD ORDER IN \( \lambda \)

Here we give the results of expanding the magnetizations and two- and three-point correlations, (7), to third order in \( \lambda \).

1. Magnetizations

Continuing expansion (7) for the magnetizations to third order in \( \lambda \), we find

\[
m_i = \tanh \left( h_i + \sum_{j=1}^{N} J_{ij} m_j - m_i a_i + \frac{2}{3} (1 - 3m_i^3) b_i - m_i c_i \right),
\]

where we have defined the auxiliary quantities

\[
a_i = \sum_{j=1}^{N} J_{ij}^2 (1 - m_j^3),
\]

\[
b_i = \sum_{j=1}^{N} J_{ij} m_j (1 - m_j^3),
\]

\[
c_i = \sum_{j,k=1 \atop j \neq k}^{N} J_{ij} (1 - m_j^3) J_{jk} (1 - m_k^3) J_{ijk}^{\text{sym}},
\]

and \( J_{ijk}^{\text{sym}} = (J_{ij} + J_{ji})/2 \) denotes the entry of the symmetric part of the coupling matrix.

2. Two- and three-point correlations under sequential dynamics

We denote the two- and three-point correlations computed to second order in \( \lambda \) as \( C_{ij}^{\text{TAP}} \) and \( C_{ijk}^{TAP} \), respectively. Their expressions are given in the text.

For the third-order correction to the two-point correlations we obtain

\[
C_{ij} - C_{ij}^{\text{TAP}} = (1 - m_i^2)(1 - m_j^2) \times \left\{ \frac{1}{3} J_{ij}^3 (1 - 3m_i^2)(1 - 3m_j^2) + 2m_i m_j J_{ij} A_{ij} - \frac{1}{2} J_{ij} (1 - m_j^2) a_i + \frac{1}{2} m_i F_{ij} + \frac{1}{2} E_{ij} \right\}
\]

\( (i \neq j) \),

where we have defined the auxiliary quantities

\[
A_{ij} = \sum_{k=1 \atop k \neq i}^{N} J_{ik}^{\text{sym}} J_{jk} (1 - m_k^2),
\]

\[
E_{ij} = \sum_{k=1 \atop k \neq i}^{N} A_{ik} + A_{ki} J_{jk} (1 - m_k^2),
\]

\[
F_{ij} = \sum_{k=1 \atop k \neq i}^{N} (J_{ik}^2 + J_{jk}^2) J_{jk} (1 - m_k^2) m_k.
\]

\( a_i \) are defined in (A2).

For the third-order correction to the three-point correlations we find

\[
C_{ijk} - C_{ijk}^{\text{TAP}} = \frac{(1 - m_i^2)(1 - m_j^2)(1 - m_k^2)}{3} \times \left\{ -J_{ij}^{\text{sym}} \left[ 4 J_{ik} J_{jk} m_i m_j m_k + 4 m_k (J_{ik}^2 m_k^3) \right] + 2 J_{ik} m_i \left[ (1 - 3m_i^2) J_{ik} J_{jk} - m_i m_j (J_{ij}^2 + J_{ji}^2) - A_{ij} \right] - 2m_k \sum_{l=1 \atop l \neq i,j}^{N} J_{il} (1 - m_l^2) J_{il} J_{ijk}^{\text{sym}} \right\}
\]

\( + \sum_{l=1 \atop l \neq i,j}^{N} \frac{J_{il}}{2} \left( \frac{C_{ij}^{\text{TAP}}}{(1 - m_i^2)(1 - m_j^2)} \right) \)

\( + \) permutations of \( (i,j,k) \).

APPENDIX B: DESCRIPTION OF THE PARAMETER INFERENCE ALGORITHM

In order to reconstruct the model parameters, we consider Eqs. (3) and (4) for the magnetizations and two- and three-point correlations and solve for the couplings and external fields. Our goal is to minimize the relative squared error of the predictions,
which leads us to define the cost function

\[ E(h, J) = \frac{\|m^\ast(h, J) - m_{\text{sampled}}\|^2_2}{\|m_{\text{sampled}}\|^2_2} + \frac{\|C_{ij}^\ast(h, J) - C_{ij}_{\text{sampled}}\|^2_2}{\|C_{ij}_{\text{sampled}}\|^2_2} + \frac{\|C_{ijk}^\ast(h, J) - C_{ijk}_{\text{sampled}}\|^2_2}{\|C_{ijk}_{\text{sampled}}\|^2_2} \]

(B1)

and its mean-field approximation

\[ E_{\text{MF}}(J) = \frac{\|C_{ij}^{\ast}\text{MF}(J) - C_{ij}_{\text{sampled}}\|^2_2}{\|C_{ij}_{\text{sampled}}\|^2_2} + \frac{\|C_{ijk}^{\ast}\text{MF}(J) - C_{ijk}_{\text{sampled}}\|^2_2}{\|C_{ijk}_{\text{sampled}}\|^2_2} \]

(B2)

where the \( l_2 \) norm \( \| \|_2 \) for the symmetric correlation tensors is defined as the sum over the squared independent entries \( \|X_{ij}\|^2_2 = \sum_{i<j} X_{ij}^2 \) and \( \|X_{ijk}\|^2_2 = \sum_{i<j<k} X_{ijk}^2 \) and the indices sc and MF denote the exact self-consistent equations (3) and (4), and the explicit mean-field expressions (9), (A5) and (10), (A9), respectively.

These cost functions are nonnegative functions of the model parameters; they are 0 when the connected two- and three-point correlations (and magnetizations for the exact inference) exactly match the empirically measured correlations (and magnetizations). The mean-field cost function only depends on the coupling matrix \( J \) since the reconstruction of the fields is independent of the coupling inference and is done by solving the magnetization equation (A1), with the reconstructed couplings. The cost functions (B1) and (B2), can be viewed as formal energies to be minimized by some algorithm.

Our inference problem can now be restated as finding \((h^*, J^*)_{\text{exact}} = \arg\min_{h, J} E(h, J)\) for the exact inference or \( J_{\text{MF}} = \arg\min_{J} E_{\text{MF}}(J) \). We use the Levenberg-Marquardt algorithm [18,19] as implemented in the Python library SciPy [20] as a numerical solver. We find that the energy landscapes exhibit many local minima. For this reason it is not sufficient to use a single starting point for the solver. Instead we use 100 random starting points drawn from the same distribution as the model parameters. For each of these starting points, the Levenberg-Marquardt algorithm finds a local minimum, and of these candidates we choose the one with the lowest energy.