

Mishchenko, Yuriy

Consistent estimation of complete neuronal connectivity in large neuronal populations using sparse “shotgun” neuronal activity sampling. (English) [Zbl 1382.92070](#)
J. Comput. Neurosci. 41, No. 2, 157-184 (2016).

Summary: We investigate the properties of recently proposed “shotgun” sampling approach for the common inputs problem in the functional estimation of neuronal connectivity. We study the asymptotic correctness, the speed of convergence, and the data size requirements of such an approach. We show that the shotgun approach can be expected to allow the inference of complete connectivity matrix in large neuronal populations under some rather general conditions. However, we find that the posterior error of the shotgun connectivity estimator grows quickly with the size of unobserved neuronal populations, the square of average connectivity strength, and the square of observation sparseness. This implies that the shotgun connectivity estimation will require significantly larger amounts of neuronal activity data whenever the number of neurons in observed neuronal populations remains small. We present a numerical approach for solving the shotgun estimation problem in general settings and use it to demonstrate the shotgun connectivity inference in the examples of simulated synfire and weakly coupled cortical neuronal networks.

MSC:

92C20 Neural biology

62P10 Applications of statistics to biology and medical sciences; meta analysis

60J22 Computational methods in Markov chains

Keywords:

functional connectivity; neuronal circuit reconstruction; calcium imaging; neuronal population activity

Full Text: [DOI](#)

References:

- [1] Abeles, M. (1991). *Corticonics*: Cambridge University Press.
- [2] Bellet, L.R. (2006). Ergodic properties of Markov processes. In *Open Quantum Systems II* (pp. 1-39). Berlin: Springer. · [Zbl 1126.60057](#)
- [3] Berk, KN, A central limit theorem for m-dependent random variables with unbounded m, *Annals of Probability*, 1, 352-354, (1973) · [Zbl 0263.60006](#) · [doi:10.1214/aop/1176996992](#)
- [4] Boyd, S.P. (2004). *Convex optimization*: Cambridge University Press. · [Zbl 1058.90049](#)
- [5] Bradley, RC, Basic properties of strong mixing conditions. A survey and some open questions, *Probability surveys*, 2, 107-144, (2005) · [Zbl 1189.60077](#) · [doi:10.1214/154957805100000104](#)
- [6] Braitenberg, V., & Schuz, A. (1998). *Cortex: statistics and geometry of neuronal connectivity*. Berlin: Springer. · [doi:10.1007/978-3-662-03733-1](#)
- [7] Brillinger, D, Maximum likelihood analysis of spike trains of interacting nerve cells, *Biological Cybernetics*, 59, 189-200, (1988) · [Zbl 0646.92007](#) · [doi:10.1007/BF00318010](#)
- [8] Brillinger, D, Nerve cell spike train data analysis: a progression of technique, *Journal of the American Statistical Association*, 87, 260-271, (1992) · [doi:10.1080/01621459.1992.10475205](#)
- [9] Chornoboy, E; Schramm, L; Karr, A, Maximum likelihood identification of neural point process systems, *Biological Cybernetics*, 59, 265-275, (1988) · [Zbl 0658.92007](#) · [doi:10.1007/BF00332915](#)
- [10] Cotton, RJ; Froudarakis, E; Storer, P; Saggau, P; Tolia, AS, Three-dimensional mapping of microcircuit correlation structure, *Frontiers in Neural Circuits*, 7, 151, (2013) · [doi:10.3389/fncir.2013.00151](#)
- [11] Cossart, R; Aronov, D; Yuste, R, Attractor dynamics of network up states in the neocortex, *Nature*, 423, 283-288, (2003) · [doi:10.1038/nature01614](#)
- [12] Coulon-Prieur, C; Doukhan, P, A triangular central limit theorem under a new weak dependence condition, *Stat. Probab. Lett.*, 27, 61-68, (2000) · [Zbl 0956.60006](#) · [doi:10.1016/S0167-7152\(99\)00138-8](#)
- [13] Davidson, J. (2006). Asymptotic methods and functional central limit theorems. In T.C. Mills, & K. Patterson (Eds.), *Palgrave Handbooks of Econometrics*: Palgrave-Macmillan.
- [14] Dedecker, J; Merlevede, F, Necessary and sufficient conditions for the conditional central limit theorem, *Annals of Probability*, 30, 1044-1081, (2002) · [Zbl 1015.60016](#) · [doi:10.1214/aop/1029867121](#)

- [15] Dempster, A; Laird, N; Rubin, D, Maximum likelihood from incomplete data via the EM algorithm, *Journal of the Royal Statistical Society, Series B*, 39, 1-38, (1977) · [Zbl 0364.62022](#)
- [16] Djuricic, M; Antic, S; Chen, WR; Zecevic, D, Voltage imaging from dendrites of mitral cells: EPSP attenuation and spike trigger zones, *Journal of Neuroscience*, 24, 6703-6714, (2004) · [doi:10.1523/JNEUROSCI.0307-04.2004](#)
- [17] Furedi, Z; Komlos, J, The eigenvalues of random symmetric matrices, *Combinatorica*, 1, 233, (1981) · [Zbl 0494.15010](#) · [doi:10.1007/BF02579329](#)
- [18] Doukhan, P. (1994). *Mixing: Properties and Examples*: Springer. *Lect. Notes. Stat.* 85. · [Zbl 0801.60027](#)
- [19] Godsill, S; Doucet, A; West, M, Maximum a posteriori sequence estimation using Monte Carlo particle filters, *Annals of the Institute of Statistical Mathematics*, 53, 82-96, (2001) · [Zbl 0995.62096](#) · [doi:10.1023/A:1017968404964](#)
- [20] Gomez-Urquijo, SM; Reblet, C; Bueno-Lopez, JL; Gutierrez-Ibarluzea, I, Gabaergic neurons in the rabbit visual cortex: percentage, distribution and cortical projections, *Brain Research*, 862, 171-9, (2000) · [doi:10.1016/S0006-8993\(00\)02114-4](#)
- [21] Grewe, B., Langer, D., Kasper, H., Kampa, B., & Helmchen, F. (2010). High-speed *in vivo* calcium imaging reveals neuronal network activity with near-millisecond precision. *Nature Methods*, 399-405. · [Zbl 1015.60016](#)
- [22] Guillotin-Plantard, N; Prieur, C, Central limit theorem for sampled sums of dependent random variables, *ESAIM: Probability and Statistics*, 14, 299-314, (2010) · [Zbl 1219.60023](#) · [doi:10.1051/ps:2008030](#)
- [23] Hairer, M. (2010). "Convergence of Markov processes." *Lecture notes*.
- [24] Hall, P., & Heyde, C.C. (2014). *Martingale limit theory and its applications*, (p. 320): Academic Press. Chapter 3. · [Zbl 0462.60045](#)
- [25] Iyer, V; Hoogland, TM; Saggau, P, Fast functional imaging of single neurons using random-access multiphoton (RAMP) microscopy, *Journal of Neurophysiology*, 95, 535-545, (2006) · [doi:10.1152/jn.00865.2005](#)
- [26] Johnson, O, An information-theoretic central limit theorem for finitely susceptible FKG systems, *Theory Probab. Appl.*, 50, 214-224, (2001) · [Zbl 1331.60049](#) · [doi:10.1137/S0040585X97981676](#)
- [27] Kantas, N., Doucet, A., Singh, S.S., & Maciejowski, J.H. (2009). An overview of sequential Monte Carlo methods for parameter estimation in general state-space models. In *15th IFAC Symposium on System Identification (SYSID)*, Saint-Malo, France, 2009 Jul 6}, (Vol. 102 p. 117).
- [28] Keshri, S., Pnevmatikakis, E., Pakman, A., Shababo, B., & Paninski, L. (2013). A shotgun sampling solution for the common input problem in neuronal connectivity inference. [arXiv:http://arxiv.org/abs/1309.3724](http://arxiv.org/abs/1309.3724). · [Zbl 1331.62161](#)
- [29] Klartag, B, A central limit theorem for convex sets, *Inventiones Mathematicae*, 168, 91-131, (2007) · [Zbl 1144.60021](#) · [doi:10.1007/s00222-006-0028-8](#)
- [30] Koch, C. (1999). *Biophysics of Computation*: Oxford University Press.
- [31] Kulkarni, J; Paninski, L, Common-input models for multiple neural spike-train data, *Network: Computation in Neural Systems*, 18, 375-407, (2007) · [doi:10.1080/09548980701625173](#)
- [32] Lefort, S; Tamm, C; Floyd Sarria, J-C; Petersen, CCH, The excitatory neuronal network of the c2 barrel column in mouse primary somatosensory cortex, *Neuron*, 61, 301-16, (2009) · [doi:10.1016/j.neuron.2008.12.020](#)
- [33] Lehmann, E.L. (1999). *Elements of large-sample theory*. New York: Springer. Chapter 2.8. · [Zbl 0914.62001](#) · [doi:10.1007/b98855](#)
- [34] Mishchenko, Y; Vogelstein, J; Paninski, L, A Bayesian approach for inferring neuronal connectivity from calcium fluorescent imaging data, *Annals of Applied Statistics*, 5, 1229-61, (2011) · [Zbl 1223.62162](#) · [doi:10.1214/09-AOAS303](#)
- [35] Mishchenko, Y; Paninski, L, Efficient methods for sampling spike trains in networks of coupled neurons, *The Annals of Mathematical Statistics*, 5, 1893-1919, (2011) · [Zbl 1229.92015](#)
- [36] Newman, C. (1984). Asymptotic Independence and Limit Theorems for Positively and Negatively Dependent Random Variables. *Lecture Notes-Monograph Series*, 127-140. · [Zbl 1219.60023](#)
- [37] Neumann, MH, A central limit theorem for triangular arrays of weakly dependent random variables, with applications in statistics, *ESAIM: Probability and Statistics*, 17, 120-134, (2013) · [Zbl 1291.60047](#) · [doi:10.1051/ps/2011144](#)
- [38] Nguyen, QT; Callamaras, N; Hsieh, C; Parker, I, Construction of a two-photon microscope for video-rate ca²⁺ imaging, *Cell Calcium*, 30, 383-393, (2001) · [doi:10.1054/ceca.2001.0246](#)
- [39] Nykamp, D, A mathematical framework for inferring connectivity in probabilistic neuronal networks, *Mathematical Biosciences*, 205, 204-251, (2007) · [Zbl 1109.92004](#) · [doi:10.1016/j.mbs.2006.08.020](#)
- [40] Nykamp, DQ, Revealing pairwise coupling in linear-nonlinear networks, *SIAM Journal of Applied Mathematics*, 65, 2005-2032, (2005) · [Zbl 1077.92011](#) · [doi:10.1137/S0036139903437072](#)
- [41] Ohki, K; Chung, S; Ch'ng, Y; Kara, P; Reid, C, Functional imaging with cellular resolution reveals precise micro-architecture in visual cortex, *Nature*, 433, 597-603, (2005) · [doi:10.1038/nature03274](#)
- [42] Paninski, L, Maximum likelihood estimation of cascade point-process neural encoding models, *Network: Computation in Neural Systems*, 15, 243-262, (2004) · [doi:10.1088/0954-898X154002](#)
- [43] Paninski, L; Ahmadian, Y; Ferreira, D; Koyama, S; Rahnama, K; Vidne, M; Vogelstein, J; Wu, W, A new look at state-space models for neural data, *Journal of Computational Neuroscience*, 29, 107-126, (2010) · [doi:10.1007/s10827-009-0179-x](#)
- [44] Paninski, L; Fellows, M; Shoham, S; Hatsopoulos, N; Donoghue, J, Superlinear population encoding of dynamic hand trajectory in primary motor cortex, *Journal of Neuroscience*, 24, 8551-8561, (2004) · [Zbl 0949.44001](#) · [doi:10.1523/JNEUROSCI.0919-04.2004](#)
- [45] Pillow, J., & Latham, P. (2007). Neural characterization in partially observed populations of spiking neurons. *NIPS*.

- [46] Pillow, J; Shlens, J; Paninski, L; Sher, A; Litke, A; Chichilnisky, E; Simoncelli, E, Spatiotemporal correlations and visual signaling in a complete neuronal population, *Nature*, 454, 995-999, (2008) · doi:10.1038/nature07140
- [47] Plesser, H; Gerstner, W, Noise in integrate-and-fire neurons: from stochastic input to escape rates, *Neural Computation*, 12, 367-384, (2000) · doi:10.1162/089976600300015835
- [48] Rabiner, LR, A tutorial on hidden Markov models and selected applications in speech recognition, *Proceedings of the IEEE*, 72, 257-286, (1989) · doi:10.1109/5.18626
- [49] Rasmussen, C.E., & Williams, C.K.I. (2006). *Gaussian processes for Machine Learning*. MIT Press: Appendix B.
- [50] Reddy, G., Kelleher, K., Fink, R., & Saggau, P. (2008a). Three-dimensional random access multiphoton microscopy for functional imaging of neuronal activity. *Nature neuroscience*, 11, 713-720.
- [51] Reddy, G., Kelleher, K., Fink, R., & Saggau, P. (2008b). Three-dimensional random access multiphoton microscopy for functional imaging of neuronal activity. *Nature Neuroscience*, 11(6), 713-720. · Zbl 1219.60023
- [52] Rigat, F; de Gunst, M; van Pelt, J, Bayesian modelling and analysis of spatio-temporal neuronal networks, *Bayesian Analysis*, 1, 733-764, (2006) · Zbl 1331.62161 · doi:10.1214/06-BA124
- [53] Salome, R; Kremer, Y; Dieudonne, S; Leger, J-F; Krichevsky, O; Wyart, C; Chatenay, D; Bourdieu, L, Ultrafast random-access scanning in two-photon microscopy using acousto-optic deflectors, *Journal of Neuroscience Methods*, 154, 161-174, (2006) · doi:10.1016/j.jneumeth.2005.12.010
- [54] Sayer, RJ; Friedlander, MJ; Redman, SJ, The time course and amplitude of epsps evoked at synapses between pairs of ca3/ca1 neurons in the hippocampal slice, *Journal of Neuroscience*, 10, 826-36, (1990)
- [55] Soudry, D; Keshri, S; Stinson, P; Oh, M-H; Iyengar, G; Paninski, L, Efficient “shotgun” inference of neural connectivity from highly sub-sampled activity data, *PLOS Computational Biology*, 11, e1004464, (2015) · doi:10.1371/journal.pcbi.1004464
- [56] Stevenson, I., Rebesco, J., Hatsopoulos, N., Haga, Z., Miller, L., & Koerding, K. (2008a). Inferring network structure from spikes. *Statistical Analysis of Neural Data meeting*. · Zbl 0364.62022
- [57] Stevenson, IH; Rebesco, JM; Hatsopoulos, NG; Haga, Z; Miller, LE; Kording, KP, Bayesian inference of functional connectivity and network structure from spikes, *IEEE Transactions on Neural Systems and Rehabilitation*, 17, 203-13, (2009) · doi:10.1109/TNSRE.2008.2010471
- [58] Stevenson, I.H., Rebesco, J.M., Miller, L.E., & Kording, K.P. (2008b). Inferring functional connections between neurons. *Current Opinion in Neurobiology*, 18, 582-8.
- [59] Stosiek, C; Garaschuk, O; Holthoff, K; Konnerth, A, In vivo two-photon calcium imaging of neuronal networks, *Proceedings of The National Academy Of Sciences Of The United States Of America*, 100, 7319-7324, (2003) · doi:10.1073/pnas.1232232100
- [60] Theis, L., Berens, P., Froudarakis, E., Reimer, J., Roman-Roson, M., Baden, T., Euler T., Tolia A.S., & Bethge, M. (2015). Supervised learning sets benchmark for robust spike detection from calcium imaging signals. *bioRxiv*, 010777.
- [61] Truccolo, W; Eden, U; Fellows, M; Donoghue, J; Brown, E, A point process framework for relating neural spiking activity to spiking history, neural ensemble and extrinsic covariate effects, *Journal of Neurophysiology*, 93, 1074-1089, (2005) · doi:10.1152/jn.00697.2004
- [62] Tsien, RY, Fluorescent probes of cell signaling, *Annual Review of Neuroscience*, 12, 227-253, (1989) · doi:10.1146/annurev.ne.12.030189.001303
- [63] Turaga, S., Buesing, L., Packer, A., Dalgleish, H., Pettit, N., Hausser, M., & Macke, J. (2013). Inferring neural population dynamics from multiple partial recordings of the same neural circuit. *NIPS*.
- [64] Varadhan, S.R.S. (2001). *Probability theory, volume 7 of Courant Lecture Notes in Mathematics*. New York: New York University Courant Institute of Mathematical Sciences. Chapter 6. · Zbl 0980.60002
- [65] Vidne, M; Ahmadian, Y; Shlens, J; Pillow, J; Kulkarni, J; Litke, A; Chichilnisky, E; Simoncelli, E; Paninski, L, The impact of common noise on the activity of a large network of retinal ganglion cells, *Journal of Computational Neuroscience*, 33, 97-121, (2012) · doi:10.1007/s10827-011-0376-2
- [66] Vidne, M., Kulkarni, J., Ahmadian, Y., Pillow, J., Shlens, J., Chichilnisky, E., Simoncelli, E., & Paninski, L. (2009). Inferring functional connectivity in an ensemble of retinal ganglion cells sharing a common input. *COSYNE*.
- [67] Vogelstein, J; Watson, B; Packer, A; Yuste, R; Jedynek, B; Paninski, L, Spike inference from calcium imaging using sequential Monte Carlo methods, *Biophysical Journal*, 97, 636, (2009) · doi:10.1016/j.bpj.2008.08.005
- [68] Vogelstein, JT; Packer, AM; Machado, TA; Sippy, T; Babadi, B; Yuste, R; Paninski, L, Fast nonnegative deconvolution for spike train inference from population calcium imaging, *Journal of Neurophysiology*, 104, 3691, (2010) · doi:10.1152/jn.01073.2009
- [69] Wallace, D; zum Alten Borgloh, S; Astori, S; Yang, Y; Bausen, M; Kugler, S; Palmer, A; Tsien, R; Sprengel, R; Kerr, J; Denk, W; Hasan, M, Single-spike detection in vitro and in vivo with a genetic ca2+ sensor, *Nature Methods*, 5, 797-804, (2008) · doi:10.1038/nmeth.1242
- [70] Yatsenko, D; Josi, K; Ecker, AS; Froudarakis, E; Cotton, RJ; Tolia, AS, Improved estimation and interpretation of correlations in neural circuits, *PLoS Computational Biology*, 11, e1004083, (2015) · doi:10.1371/journal.pcbi.1004083
- [71] Yuste, R., Konnerth, A., Masters, B., & et al. (2006). *Imaging in Neuroscience and Development, A Laboratory Manual*. · Zbl 0658.92007

This reference list is based on information provided by the publisher or from digital mathematics libraries. Its items are heuristically matched to zbMATH identifiers and may contain data conversion errors. It attempts to reflect the references listed in the original paper as accurately as possible without claiming the completeness or perfect precision of the matching.