How advances in neural recording affect data analysis

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Supplementary Table 1

Neurons	*Year*	*Reference*
2	1961	Amassian, V. E., et al. (1961). *Annals of the New York Academy of Sciences.*
2	1963	Griffith, J. S. and G. Horn (1963). *Nature*.
2	1964	Braitenberg, V., et al. (1965). *Biological Cybernetics.*
2	1965	Evarts, E. V. (1965). *Journal of Neurophysiology.*
2	1965	Oikawa, T., et al. (1965). *Yonago acta medica.*
2	1970	Noda, H. and W. R. Adey (1970). *Journal of Neurophysiology.*
2	1974	Dickson, J. W. and G. L. Gerstein (1974). *Journal of Neurophysiology.*
3	1959	Amassian, V. E., et al. (1959). *Trans. NY Acad. Sci.*
3	1972	Gerstein, G. L. and D. H. Perkel (1972). *Biophysical Journal.*
3	1977	Loeb, G. E., et al. (1977). *Science.*
4	1984	Frostig, R. D., et al. (1984). *Brain Research.*
5	1983	McNaughton, B. L., et al. (1983). *Journal of Neuroscience Methods.*
6	1982	Krüger, J. (1982). *Journal of Neuroscience Methods.*
7	1978	Durelli, L., et al. (1978). *Experimental Neurology.*
7	1982	Reitboeck, H. J. and G. Werner (1983). *Cellular and Molecular Life Sciences.*
7	1985	Legendy, C. R. and M. Salcman (1985). *Journal of Neurophysiology.*
8	1987	Lindsey, B. G., et al. (1987). *Journal of Neurophysiology.*
8	1988	Abeles, M. and G. L. Gerstein (1988). *Journal of Neurophysiology.*
9	1973	Salcman, M. and M. J. Bak (1973). *IEEE Transactions on Biomedical Engineering.*
9	1988	Lindsey, B. G., et al. (1989). *Brain Research.*
10	1990	Mountcastle, V. B., et al. (1991). *Journal of Neuroscience Methods.*
10	1993	Abeles, M., et al. (1993). *Journal of Neurophysiology.*
11	1990	Ahissar, E. and E. Vaadia (1990). *PNAS.*
12	1976	Schmidt, E. M., et al. (1976). *Experimental Neurology.*
14	1988	Mioche, L. and W. Singer (1988). *Journal of Neuroscience Methods.*
15	1981	Krüger, J. and M. Bach (1981). *Experimental Brain Research.*
15	1999	Villa, A. E. P., et al. (1999). *Proceedings of the National Academy of Sciences.*
16	1995	Vaadia, E., et al. (1995). *Nature.*
16	1998	Prut, Y., et al. (1998). *Journal of Neurophysiology.*
19	1988	Eckhorn, R., et al. (1988). *Biological Cybernetics.*
19	2004	Laubach, M., et al. (2000). *Nature.*
23	1999	Chapin, J. K. and M. A. L. Nicolelis (1999). *Journal of Neuroscience Methods.*
30	2000	Isaacs, R. E., et al. (2000). *IEEE Transactions on Rehabilitation Engineering.*
31	2000	Chang, J. Y., et al. (2000). *Neuroscience.*
32	1998	Chang, J. Y., et al. (1997). *Brain Research.*
32	2001	Giszter, S. F., et al. (2001). *Robotics and Autonomous Systems.*
35	1999	Nicolelis, M., et al. (1998). *Methods for Neural Ensemble Recordings.*
46	1999	Chapin, J. K., et al. (1999). *Nature Neuroscience.*
48	1995	Nicolelis, M. A., et al. (1995). *Science.*
55	2004	Patil, P. G., et al. (2004). *Neurosurgery.*
60	2004	Stein, R. B., et al. (2004). *The Journal of Physiology.*
64	2002	Taylor, D. M., et al. (2002). *Science.*
68	2007	Hatsopoulos, N. G., et al. (2007). *Journal of Neuroscience.*
90	2003	Carmena, J. M., et al. (2003). *PLoS Biol.*
100	1997	Nicolelis, M. A. L., et al. (1997). *Neuron.*
100	2000	Wessberg, J., et al. (2000). *Nature.*
107	2009	Winzenborg, I., et al. (2009). *Journal of Computational Neuroscience.*
119	2009	Nuding, S. C., et al. (2009). *Journal of Neurophysiology.*
140	2007	Hamed, S. B., et al. (2007). *Journal of Neurophysiology.*
143	2004	Hatsopoulos, N., et al. (2004). *Journal of Neurophysiology.*
147	2005	Santucci, D. M., et al. (2005). *European Journal of Neuroscience.*
177	2005	Lebedev, M. A., et al. (2005). *Journal of Neuroscience.*
183	2007	Zacksenhouse, M., et al. (2007). *PLoS ONE.*
185	2004	Sanchez, J. C., et al. (2004). *IEEE Transactions on Biomedical Engineering.*
192	2009	Kim, S. P., et al. (2008). *Journal of neural engineering.*
247	2003	Nicolelis, M. A. L., et al. (2003). *PNAS.*

Table S1: List of papers used to generate Fig 1a – found using an in-depth literature search and an informal survey of researchers in the field.

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Supplementary Methods

We quantified the growth of neural recording methods using an in-depth search of the literature. Representative papers were found by searching Google Scholar for the phrases "N simultaneously recorded neurons", "simultaneously recorded N neurons", or "N neurons were recorded simultaneously." For older literature we informally surveyed several researchers who provided lists of relevant papers. Since we are primarily interested in the growth of number of neurons recorded, we selected the first M papers to report simultaneous recordings from at least N neurons. M = 1, for instance, would only include a paper if no other paper had previously recorded from more neurons. M = 10 (used here) provided a balance between using enough data and not overweighting recent papers with relatively few simultaneously recorded neurons. The estimates of doubling time therefore reflect the upper-range of simultaneously recorded neurons rather than the average. The estimated doubling time was robust to the value of M, and confidence intervals overlapped for all values tested. A complete list of papers used can be found above (Table S1).

To fit spike data recorded from motor and visual cortices we used two types of generalized linear models for trial-by-trial, spike count data. Data from motor cortex were recorded while a monkey performed a randomized, eight-target, center-out reaching task (see [1] for details). Trial-by-trial spike counts were collected during the period 100–300ms following movement onset from 315 trials, and the average firing rate in this period for all neurons was 8.1 ± 0.7 Hz. Data from visual cortex were recorded while an anesthetized monkey viewed one of eight randomly oriented, drifting sine-wave gratings (see [2] for details). Stimuli had a spatial frequency of 1 cyc/deg, drift rate of 6.25 cyc/s, size of 2.9 deg and were presented for 400 ms with a 800 ms delay between stimuli. Trial-by-trial spike counts were collected for the entire 400 ms stimulus period for 3200 trials (400 repetitions for each orientation). The average firing rate during stimulus presentation was 14.6 ± 0.9 Hz across neurons. Both datasets used only well-isolated single units, with firing rates > 1Hz.

Spike count data were fit using either the stimulus/movement direction or the activity of the other recorded neurons[3-6]. In both cases we use a class of generalized linear model[7] often called linear non-linear Poisson (LNLP) models[8-9]. The model and estimation methods have been previously described in detail elsewhere[5]. Briefly, we assume that the covariates (stimulus/movement direction or activity of other neurons) are linearly combined, then passed through an exponential nonlinearity such that the firing rate is non-negative. For the tuning curve model we assume that the conditional intensity (firing rate) of each neuron depends on hand direction or grating orientation as

$$\lambda_i(t \mid \boldsymbol{\alpha}, \theta_t) = \exp(\left[1 \ \cos\theta_t \ \sin\theta_t\right]\boldsymbol{\alpha})$$

Where θ_t is the orientation/direction for trial t and the parameter vector α determines the baseline firing rate, modulation, and preferred direction. For the interaction model we assume that the conditional intensity of each neuron depends on the activity of the other recorded neurons

$$\lambda_i(t \mid \boldsymbol{\alpha}, N_t) = \exp(\left[1 \ n_{1,t} \ldots n_{i-1,t}, n_{i+1,t} \ldots n_{N,t}\right]\boldsymbol{\alpha})$$

Where $n_{i,t}$ represents the spike count for neuron i on trial t and, in this case, the parameter vector α determines the baseline firing rate and the influence that each of the other neurons has on our prediction. Note that the spike count for the neuron whose firing rate we are estimating is excluded. To examine the effect of network size on spike prediction accuracy we vary the total number of neurons included in the model, N, and use a random subset of all recorded neurons. For both models we then assume that spikes are generated by a Poisson random variable with this rate

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$$n_i(t) \sim Poisson(\lambda(t \mid \boldsymbol{\alpha}, X_t))$$

The parameters were fit by maximum likelihood estimation (MLE) or maximum *a posteriori* (MAP) estimation (see [5]). The tuning curve models were fit by MLE. However, since there is relatively little data (315 trials in the motor case) and the interaction model has many parameters (up to 143), there is a risk of over-fitting the data unless the parameters are constrained in some way. To reduce over-fitting in the model of neural interactions we used L1-regularization (MAP estimation), where the regularization hyper-parameter was optimized using test-set likelihood. We used jack-knifing to cross-validate both models, predicting the spike counts on each trial after fitting the other trials, and the cross-validated log-likelihood provides an estimate of how accurately we can describe neural firing under each model. The values for spike prediction accuracy reported in the main text are cross-validated log likelihood ratios between the model fits and a homogeneous Poisson process for each neuron. Values were calculated in base-2 and rescaled by time to give units of bits/s (see [5,10]).

Log likelihood ratios are typically used for model comparison and selection. It may be helpful to note that in this context, given the choice between a tuning curve model and a model of coupling, coupling is preferred if there are more than ~40 neurons in motor cortex or ~15 neurons in visual cortex. The exact point at which a coupling model gives more accurate predictions than a tuning model is determined by a number of factors, but, importantly, any deviation from exponential-cosine tuning will decrease the accuracy of the tuning models. A simple alternative would be to use a non-parametric model where the mean firing rate for each stimulus/movement direction is estimated separately or in a way that is not constrained by a parametric tuning function[11]. However, while this would increase the accuracy of the tuning model slightly, it does not change the fact that spike prediction accuracy will not grow as a function of the number of neurons when the model is based only on external covariates.

Finally, it is important to note that the scaling trend that we observe for spike prediction accuracy using a coupling model could also depend on a number of factors. Notably, we expect spike prediction accuracy to asymptote when all the relevant inputs to a neuron are being recorded. In retina for instance, coupling between retinal ganglion cells is almost entirely between nearest neighbors[5,12]. Although we observe approximately *log N* scaling of spike prediction accuracy in cortex, these data are from an incomplete, highly under-sampled set of neurons. Furthermore, this scaling trend may be influenced by the class of model used. Alternative descriptions, based on maximum entropy principles, have been examined in the context of network size[13]. However these models can be difficult to fit with large numbers of neurons and results can be difficult to interpret when the network size becomes large[14].

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