## Appendix

We briefly summarize some of the data analysis methods mentioned in the text. We denote the two values of the categorical variable (e.g., two stimulus classes in optical and functional imaging, or two response classes in receptive field or classification mapping) by the labels 0 and 1. An instance of the multivariate quantity (an "image") is denoted by a row vector *x*, consisting of *P* pixel values. We assume that class *j* (*j*=0 or 1) is associated with  $N_j$  observations of *x*; the *k*th observation is a row vector  $x_k^{[j]}$ . With these

conventions, the within-class mean for class j is given by the row vector  $\mu_j = \frac{1}{N_j} \sum_{k=1}^{N_j} x_k^{[j]}$ 

and the global mean is  $\mu = \frac{N_0 \mu_0 + N_1 \mu_1}{N_0 + N_1}$ .

The difference image is the row vector  $v_{DI} = \mu_1 - \mu_0$ .

Formally, linear regression, the Fisher discriminant, and their extensions seek specific *linear functions on images* (that is, a rule to be applied to images), not images *per se*. Operation of a linear function f on an image x can be regarded as the matrix product xf of the row vector x and the column vector f. A column vector f can be regarded as a transpose of a row (image) vector,  $f = v^T$ .

*The linear regression method* seeks a linear function  $f_{LR}$  on the set of images that provides the best prediction of the response (0 or 1).  $f_{LR} = v_{LR}^T$ , where  $v_{LR}$  is the row

(image) vector that minimizes  $\sum_{j=0}^{1} \sum_{k=1}^{N_j} \left| (x_k^{[j]} - \gamma) v_{LR}^{T} - j \right|^2.$ 

 $f_{LR} = v_{LR}^T$  may be calculated from the covariance matrix,  $S = \sum_{i=0}^{1} \sum_{k=1}^{N_j} (x_k^{[j]} - \mu)^T (x_k^{[j]} - \mu).$ 

Provided that the covariance matrix S is invertible,  $f_{LR} = \frac{N_0 N_1}{N_0 + N_1} S^{-1} (\mu_1 - \mu_0)^T$ . If the

covariance matrix is not invertible,  $v_{LR}$  is not unique.

The truncated difference method <sup>28</sup> restricts the LR estimate to the subspace spanned by the eigenvectors of *S* whose eigenvalues are within some range  $\lambda_{\min} < \lambda < \lambda_{\max}$ . (For a symmetric matrix *M*, a column vector *c* is said to be an eigenvector of *M* if  $Mc = \alpha c$  for some scalar  $\alpha$ , and  $\alpha$  is said to be the eigenvalue corresponding to *c*).

*Ridge regression* <sup>38</sup>adds a multiple of the identity to *S*, i.e., replaces *S* by  $S + \kappa I$  in the above. Other *regularization procedures* replace *S* by  $S + \kappa I + \rho C$ , where nonzero elements of *C* reflect penalties for a lack of smoothness in the estimated image  $\nu$ . Here,

 $\kappa$  and  $\rho$  are scalars, typically chosen by optimizing the ability of a model based on  $\nu$  to predict stimulus-response relationships in a separate dataset.

The *canonical variates* are the solutions of the generalized eigenvalue problem  $(\mu_1 - \mu_0)^T (\mu_1 - \mu_0) f = \lambda (S_0 + S_1) f$ ,

where  $S_0$  and  $S_1$  are the within-class covariance matrices,

$$S_{j} = \sum_{k=1}^{N_{j}} (x_{k}^{[j]} - \mu_{j})^{T} (x_{k}^{[j]} - \mu_{j}).$$

The *Fisher discriminant*<sup>27</sup> is the linear function  $f_{FD}$  on the set of images that best discriminates between the images that correspond to the two response classes. That is,  $f_{FD}$  maximizes the ratio of the projected difference between classes,  $|(\mu_1 - \mu_0)f_{FD}|^2$ , to

the projected variances within classes,  $\sum_{j=0}^{1} \sum_{k=1}^{N_j} |(x_k^{[j]} - \mu_j) f_{FD}|^2$ . For Gaussian data, this

maximum is achieved when  $f_{FD}$  is the eigenvector corresponding to the largest eigenvalue of the above generalized eigenvalue problem. Method I of the *indicator function method* <sup>30</sup>is essentially the Fisher discriminant. Method II considers multiple eigenvectors, whose eigenvalues are sufficiently large. The *generalized indicator function method* <sup>29</sup>considers eigenvectors of the more general operator  $(\mu_1 - \mu_0)^T (\mu_1 - \mu_0) - \alpha(S_0 + S_1)$  for some "quality control" parameter  $\alpha$ , adds a regularization term, and applies additional criteria to select and weight these eigenvectors.

## References

- 1. Sutter, E. in *Nonlinear Vision:Determination of Neural Receptive Fields, Function, and Networks* (eds. Pinter, R. & Nabet, B.) 171-220 (CRC Press, Cleveland, 1992).
- 2. Chichilnisky, E. J. A simple white noise analysis of neuronal light responses. *Network* 12, 199-213 (2001).
- 3. Marmarelis, P. Z. & Naka, K. White-noise analysis of a neuron chain: an application of the Wiener theory. *Science* 175, 1276-8 (1972).
- 4. Simoncelli, E., Paninski, L., Pillow, J. & Schwartz, O. in *The Cognitive Neurosciences, 3rd Edition* (ed. Gazzaniga, M.) (MIT Press, Cambridge, MA, 2004).
- 5. Touryan, J., Lau, B. & Dan, Y. Isolation of relevant visual features from random stimuli for cortical complex cells. *J Neurosci* 22, 10811-8 (2002).
- 6. Sharpee, T., Rust, N. C. & Bialek, W. Analyzing neural responses to natural signals: maximally informative dimensions. *Neural Comput* 16, 223-50 (2004).
- 7. David, S. V., Vinje, W. E. & Gallant, J. L. Natural stimulus statistics alter the receptive field structure of v1 neurons. *J Neurosci* 24, 6991-7006 (2004).
- 8. Rust, N. C., Schwartz, O., Movshon, J. A. & Simoncelli, E. P. Spatiotemporal elements of macaque v1 receptive fields. *Neuron* 46, 945-56 (2005).
- 9. Escabi, M. A. & Schreiner, C. E. Nonlinear spectrotemporal sound analysis by neurons in the auditory midbrain. *J Neurosci* 22, 4114-31 (2002).
- 10. Machens, C. K., Wehr, M. S. & Zador, A. M. Linearity of cortical receptive fields measured with natural sounds. *J Neurosci* 24, 1089-100 (2004).
- 11. Eckstein, M. P. & Ahumada, A. J., Jr. Classification images: a tool to analyze visual strategies. *J Vis 2*, 1x (2002).
- 12. Ahumada, A. J., Jr. & Lovell, J. Stimulus features in signal detection. Journal of the Acoustical Society of America 49, 1751-1756 (1971).
- 13. Grinvald, A. Optical imaging of architecture and function in the living brain sheds new light on cortical mechanisms underlying visual perception. *Brain Topogr* 5, 71-5 (1992).
- 14. Kwong, K. K. *et al.* Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci U S A* 89, 5675-9 (1992).
- 15. Ohzawa, I., DeAngelis, G. C. & Freeman, R. D. Encoding of binocular disparity by complex cells in the cat's visual cortex. *J Neurophysiol* 77, 2879-909 (1997).
- 16. Pesaran, B., Pezaris, J. S., Sahani, M., Mitra, P. P. & Andersen, R. A. Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat Neurosci* 5, 805-11 (2002).

- 17. Kenet, T., Bibitchkov, D., Tsodyks, M., Grinvald, A. & Arieli, A. Spontaneously emerging cortical representations of visual attributes. *Nature* 425, 954-6 (2003).
- 18. Rodriguez, E. *et al.* Perception's shadow: long-distance synchronization of human brain activity. *Nature* 397, 430-3. (1999).
- **19.** Lee, Y. & Schetzen, M. Measurement of the kernels of a nonlinear system by cross-correlation. *Int. J. Control* 2, 237-254 (1965).
- 20. Bialek, W. & de Ruyter van Steveninck, R. Real-time performance of a movement sensitive neuron in the blowfly visual system: coding and information transfer in short spike sequences. *Proc Roy Soc Lond B* 234, 379-414 (1988).
- 21. Victor, J. D., Shapley, R. M. & Knight, B. W. Nonlinear analysis of cat retinal ganglion cells in the frequency domain. *Proc Natl Acad Sci U S A* 74, 3068-72 (1977).
- 22. Smyth, D., Willmore, B., Baker, G. E., Thompson, I. D. & Tolhurst, D. J. The receptive-field organization of simple cells in primary visual cortex of ferrets under natural scene stimulation. *J Neurosci* 23, 4746-59 (2003).
- 23. Theunissen, F. E. *et al.* Estimating spatio-temporal receptive fields of auditory and visual neurons from their responses to natural stimuli. *Network* 12, 289-316 (2001).
- 24. Korenberg, M. J., Bruder, S. B. & McIlroy, P. J. Exact orthogonal kernel estimation from finite data records: extending Wiener's identification of nonlinear systems. *Ann Biomed Eng* 16, 201-14 (1988).
- 25. Levi, D. M. & Klein, S. A. Classification images for detection and position discrimination in the fovea and parafovea. *J Vis* 2, 46-65 (2002).
- 26. Simoncelli, E. P. & Olshausen, B. A. Natural image statistics and neural representation. *Annu Rev Neurosci* 24, 1193-216 (2001).
- 27. Fisher, R. A. The use of multiple measurements in taxonomic problems. Annals of Eugenics 7, 179-188 (1936).
- 28. Gabbay, M., Brennan, C., Kaplan, E. & Sirovich, L. A principal componentsbased method for the detection of neuronal activity maps: application to optical imaging. *Neuroimage* 11, 313-25 (2000).
- 29. Yokoo, T., Knight, B. W. & Sirovich, L. An optimization approach to signal extraction from noisy multivariate data. *Neuroimage* 14, 1309-26 (2001).
- 30. Everson, R., Knight, B. W. & Sirovich, L. Separating spatially distributed response to stimulation from background. I. Optical imaging. *Biol Cybern* 77, 407-17 (1997).
- 31. Friston, K. J., Frith, C. D., Frackowiak, R. S. & Turner, R. Characterizing dynamic brain responses with fMRI: a multivariate approach. *Neuroimage* 2, 166-72 (1995).
- 32. Worsley, K. J., Poline, J. B., Friston, K. J. & Evans, A. C. Characterizing the response of PET and fMRI data using multivariate linear models. *Neuroimage* 6, 305-19 (1997).
- 33. Bell, A. J. & Sejnowski, T. J. An information-maximization approach to blind separation and blind deconvolution. *Neural Comput* 7, 1129-59 (1995).

- 34. Thomas, C. G., Harshman, R. A. & Menon, R. S. Noise reduction in BOLDbased fMRI using component analysis. *Neuroimage* 17, 1521-37 (2002).
- 35. Carmona, R. A., Hwang, W. L. & Frostig, R. D. Wavelet analysis for brain function imaging. *IEEE Trans. on Medical Imaging* 14, 556-564 (1995).
- 36. Tikhonov, A. N. & Arsenin, V. Y. *Solutions of ill-posed problems* (Wiley, Hoboken, NJ, 1977).
- 37. Hastie, T., Buja, A. & Tibshirani, R. Penalized discriminant analysis. *Annals of Statistics* 23, 73-102 (1995).
- 38. Hastie, T., Tibshirani, R. & Friedman, J. *The elements of statistical learning: data mining, Inference, and prediction* (Springer-Verlag, New York, 2001).
- 39. Boynton, G. M., Engel, S. A., Glover, G. H. & Heeger, D. J. Linear systems analysis of functional magnetic resonance imaging in human V1. *J Neurosci* 16, 4207-21 (1996).
- 40. Paninski, L. Convergence properties of three spike-triggered analysis techniques. *Network* 14, 437-64 (2003).
- 41. Aguera y Arcas, B. & Fairhall, A. L. What causes a neuron to spike? *Neural Comput* 15, 1789-807 (2003).
- 42. Pillow, J. & Simoncelli, E. Biases in white noise analysis due to non-Poisson spike generation. *Neurocomputing* 52, 109-115 (2003).
- 43. Neri, P. Estimation of nonlinear psychophysical kernels. *J Vis* 4, 82-91 (2004).
- 44. Neri, P. & Heeger, D. J. Spatiotemporal mechanisms for detecting and identifying image features in human vision. *Nat Neurosci* 5, 812-6 (2002).
- 45. Field, D. J. Relations between the statistics of natural images and the response properties of cortical cells. *J Opt Soc Am* [A] 4, 2379-94 (1987).
- 46. Dong, D. W. & Atick, J. J. Statistics of natural time-varying images. *Network-Computation in Neural Systems* 6, 345-358 (1995).