Supp. Table 1. Biophysical properties of initial sensors with different calmodulin-binding peptides used in this study.

Supp. Table 2. Sensor variants run through cultured neuron assay.

Supp. Table 3. Crystal structure determination of jGCaMP8.410.80.

Supp. Table 4. Comparison of sensitivity and kinetics of jGCaMP8 to XCaMP-G, -Gf, and -Gf0 sensors.

Supp. Table 5. Data on electrophysiologically recorded cells.

Supp. Table 6. Biophysical characterization in purified protein.

Supp. Table 7. Statistics of the degree of nonlinearity of sensors.

Supp. Table 8. Statistics of S2F parameter fits.

Supp. Fig. 1. Crystal structure of jGCaMP8.410.80.

Supp. Fig. 2. Results of cultured neuron 1-AP field stimulation screen.

Supp. Fig. 3. Response characteristics of jGCaMP8 indicators to 1, 3, 10, and 160 field stimulation pulses.

Supp. Fig. 4. Baseline sensor brightness.

Supp. Fig. 5. Photobleaching of jGCaMP8, jGCaMP7, and XCaMP variants in neuron cell culture.

Supp. Fig. 6. Linearity of $\Delta F/F_0$ of jGCaMP8, jGCaMP7, and XCaMP variants in cultured neurons.

Supp. Fig. 7. Sensor diffusion in cultured neurons studied with fluorescence recovery after photobleaching (FRAP).

Supp. Fig. 8. jGCaMP8 sensor characterization in adult *Drosophila* L2 visual system assay.

Supp. Fig. 9. Expression of the GCaMP variants in adult fly visual system and larval neuromuscular junction.

Supp. Fig. 10. Characterization of GCaMP variants in larval neuromuscular junction.

Supp. Fig. 11. jGCaMP8f sensor characterization in larval zebrafish.

Supp. Fig. 12. Reproducible responses across trials.

Supp. Fig. 13. Response comparison between 3 weeks and 8 weeks post-AAV infection.

Supp. Fig. 14. Sensor brightness *in vivo* and expression level.

Supp. Fig. 15. Orientation selectivity of the GCaMP-expressing mice.

Supp. Fig. 16. Descriptive statistics for loose-seal cell-attached recordings.

Supp. Fig. 17. Signal-to-noise ratio of action potential recordings.

Supp. Fig. 18. Sensor fluorescence across cell body ROIs and neuropil.

Supp. Fig. 19. Effective ~500 Hz imaging of fluorescent responses *in vivo*.

Supp. Fig. 20. Responses in fast-spiking interneurons.

Supp. Fig. 21. Imaging simple and complex spikes in cerebellar Purkinje neurons.

Supp. Fig. 22. Statistics of S2F fits in the different imaging conditions.