Supporting information

**A platform to enable combined measurement of dopamine and neural activity**

**(DANA)**

Kate L. Parent[1], Daniel F. Hill[2], Lindsey M. Crown[3], Jean-Paul Wiegand[4], Kathleen F. Gies[3], Michael A. Miller[4], Christopher W. Atcherley[1], Michael L. Heien[1], Stephen L. Cowen[2]*

1. Department of Chemistry and Biochemistry, University of Arizona, Tucson, AZ 85721
2. Department of Physiology, University of Arizona, Tucson, AZ 85721
3. Department of Psychology, University of Arizona, Tucson, AZ 85721
4. Department of Neuroscience, University of Arizona, Tucson, AZ 85721

* To whom correspondence should be addressed:

PHONE: 520 626 2615
FAX: 520 626 2618
e-mail: scowen@email.arizona.edu

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**Electrode and array fabrication**

*Stereotrode array fabrication.* Stereotrodes[1] were fabricated by twisting two insulated 25 µm tungsten wires (California Fine Wire, Grover Beach CA) together. Each twisted pair was heated to fuse the insulation and increase rigidity. Sixteen fused silica capillaries (~1.5 cm long, 103 µm I.D., 170 µm O.D., Polymicro Technologies, Phoenix, AZ) were pre-loaded into eight stainless steel guide cannulae (Component Supply Company, Fort Meade, FL). Each tungsten wire pair was then inserted into one of the pre-loaded capillaries. Electrodes were connected to a custom 32-channel electrode-interface board (EIB, HTech, Tucson, AZ) fitted with a 32-channel Omnetics connector (A79032-001, Omnetics Connector Corporation, Minneapolis MN). Stereotrodes were connected to the EIB by inserting each wire into individual through-holes, each hole corresponding to a single recording channel. Wires were connected to the EIB by pressing gold EIB pins (Neuralynx, Bozeman, MT) into the through-holes to strip the electrode wire and make contact with the EIB trace.

*Carbon-fiber microelectrode fabrication*. Carbon-fiber microelectrodes were prepared as previously described.[2] In short, an AS4 carbon fiber (ø 7.4 µm, Hexcel Corporation, Stamford, CT) was loaded into a four inch glass capillary (World Precision Instruments, Inc., Sarasota, FL) then pulled to form a seal using a pipette puller (Narishige, Japan) and subsequently cut to ~ 75 µm in length.

Chronically implantable carbon-fiber microelectrodes were fabricated using the method described by Clark *et al.*[3] Briefly, an AS4 carbon fiber (Hexcel Corporation, Stamford, CT) was loaded into a ~1.5 cm length of fused silica capillary (75 µm I.D., 150 µm O.D., Polymicro Technologies). A seal was made between the carbon fiber and capillary using a quick-drying epoxy (ITW Devcon, Inc., Danvers, MA). Silver epoxy (MG Chemicals, Burlington, ON, Canada) was used to provide contact between the carbon fiber and a gold-coated pin (Newark, Chicago, IL) for interfacing. To reduce biofouling and enhance sensitivity, the electrodes were

coated in a PEDOT:Nafion polymer blend[4] by applying 15 cycles of a triangle waveform (1.5 V to -0.8 V vs. a silver quasi-reference electrode at 100 mV/s) in a 20 mL solution of acetonitrile containing 200 μM EDOT and 200 μL Nafion solution.

*Reference electrode fabrication.* The Ag/AgCl reference electrodes were produced by soaking 2.5 cm lengths of silver wire (ø 0.25 mm Alfa Aesar, Ward Hill, MA) in chlorine bleach (Food City, Chandler, AZ) for ~ 4 hours.

**Reference**


(1) McNaughton, B. L.; O'Keefe, J.; Barnes, C. A. *J. Neurosci. Methods* **1983**, *8*, 391–397.

(2) Laude, N. D.; Atcherley, C. W.; Heien, M. L. *Anal. Chem.* **2012**, *84*, 8422–8426.

(3) Clark, J. J.; Sandberg, S. G.; Wanat, M. J.; Gan, J. O.; Horne, E. A.; Hart, A. S.; Akers, C. A.; Parker, J. G.; Willuhn, I.; Martinez, V.; Evans, S. B.; Stella, N.; Phillips, P. E. M. *Nat. Methods* **2010**, *7*, 126–129.

(4) Vreeland, R. F.; Atcherley, C. W.; Russell, W. S.; Xie, J. Y.; Lu, D.; Laude, N. D.; Porreca, F.; Heien, M. L. *Anal. Chem.* **2015**, *87*, 2600–2607.

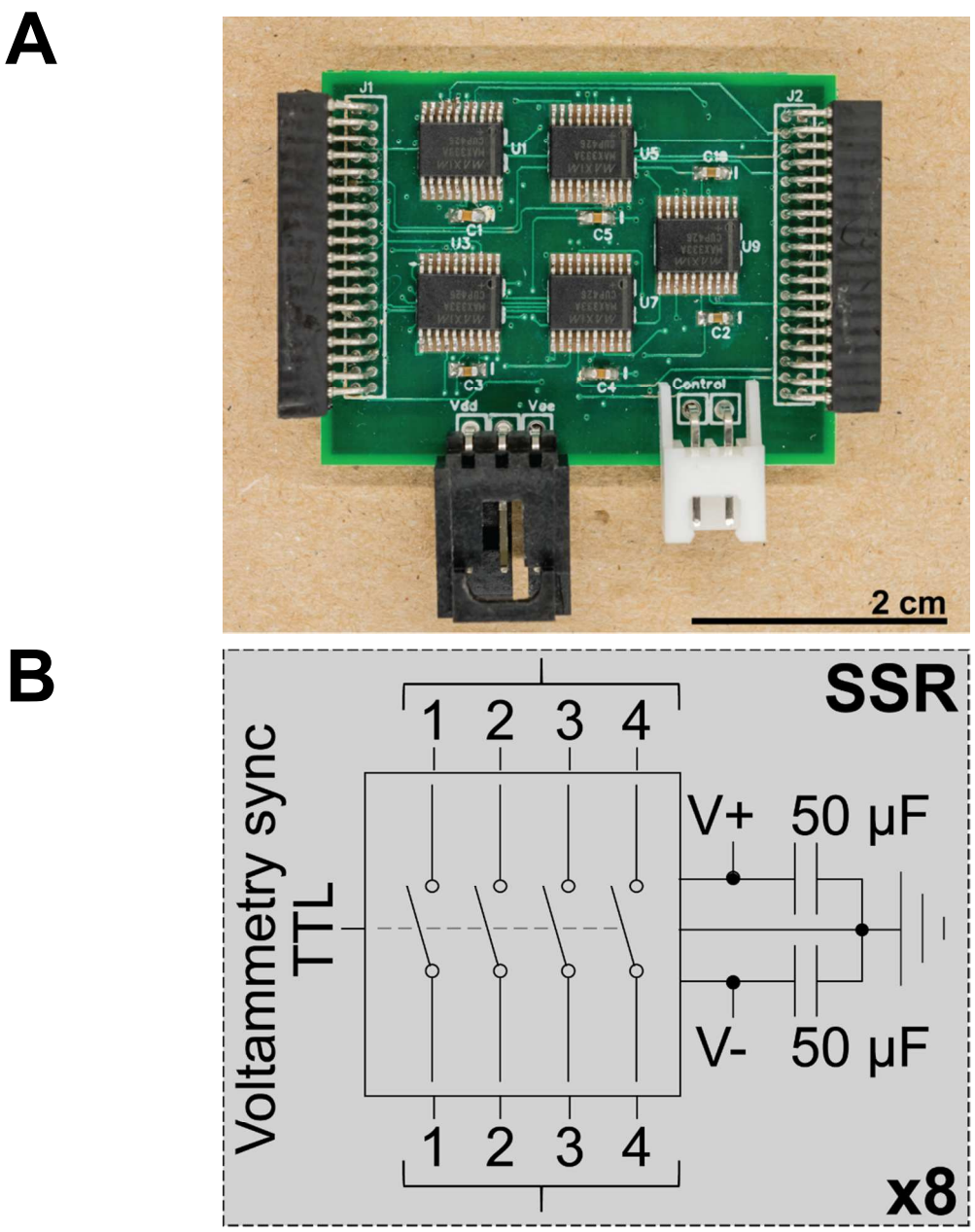


**Figure S-1.** Solid-state-relay array (SSR). (A) Photograph of the SSR. (B) Schematic of the SSR. The SSR consists of eight, four-channel MAX333A precision analog switches which prevent current flow between the electrophysiological array and amplifiers by switching to an open-circuit configuration when triggered by a TTL pulse from the voltammetric system.

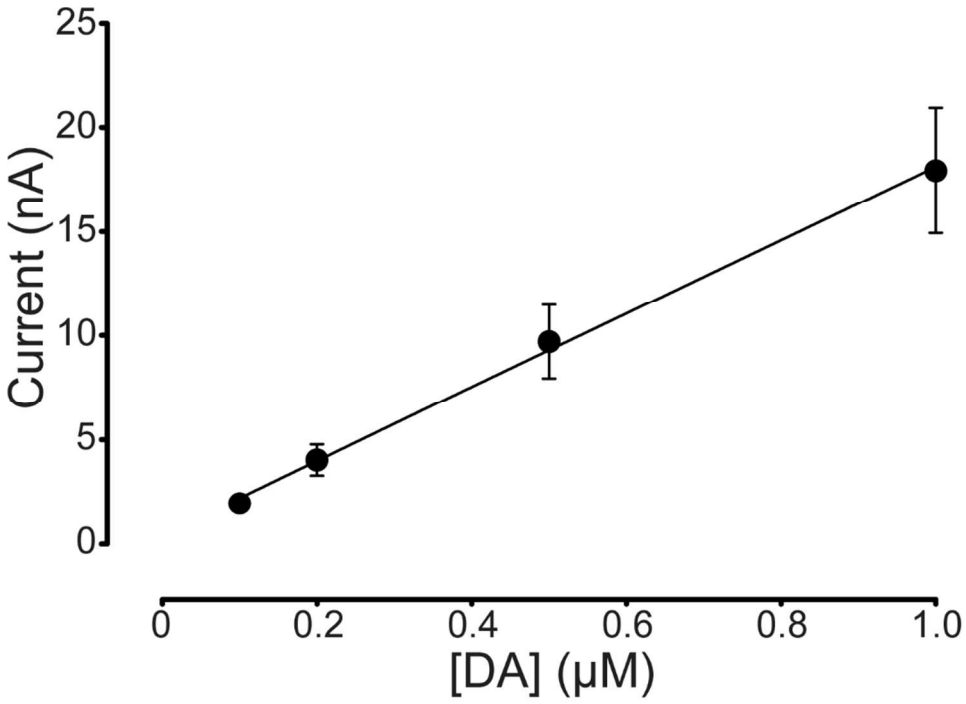


**Figure S-2.** Calibration of carbon-fiber microelectrodes. The linear fit has an $r^2$ of 0.998 and a slope of 18 nA/μM. n = 6 electrodes. Error bars signify SEM.

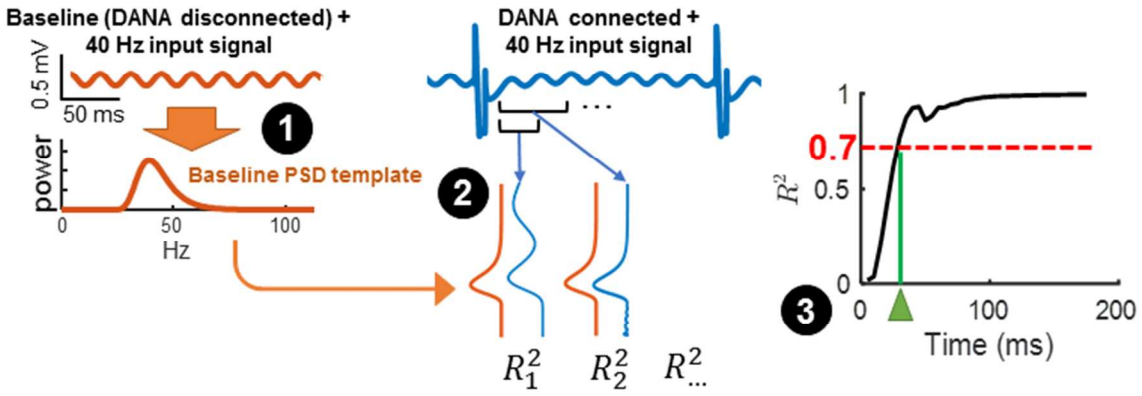


**Figure S-3.** Schematic of the template matching procedure used to quantify recovery time. (1) A baseline power spectral density (PSD) is computed from electrophysiological measurements collected when a sine-wave input signal is applied and the FSCV headstage is disconnected. (2) PSDs are computed for segments of the electrophysiological signal of increasing duration (increased by 5 ms for each increment) with the start time of all intervals beginning 5 ms following scan offset. Each of these PSDs is compared to the baseline template by calculating the Pearson correlation between the two PSDs and then squaring the outcome ($R^2$). (3) Time to recovery is defined as the time required for the $R^2$ value to exceed 0.7 (70% of variance explained by the baseline template). In this example, the time to recovery is indicated by the green triangle.

**Table S-1. Recovery time for various frequencies.**

| | | Maximum time to recover (ms) | | |
|---|---|---|---|---|
| **Signal** | **Frequency tested (Hz)** | **Uninterrupted** | **No SSR** | **SSR** |
| Theta | 5 – 10 | * | * | * |
| Beta | 10 – 20 | 135 ± 5 | 130 ± 5 | 150 ± 16 |
| Gamma | 40 – 80 | 35 ± 5 | 35 ± 5 | 45 ± 13 |
| High-frequency oscillations | 100 – 200 | 30 ± 5 | 30 ± 5 | 35 ± 15 |
| Action potentials | 1000 – 3000 | 10 ± 5 | 10 ± 5 | 10 ± 5 |

* Not recoverable within a single 200 ms scan, need multiple scans to measure these low frequencies. Error is the SEM or the sampling interval, whichever was greater.

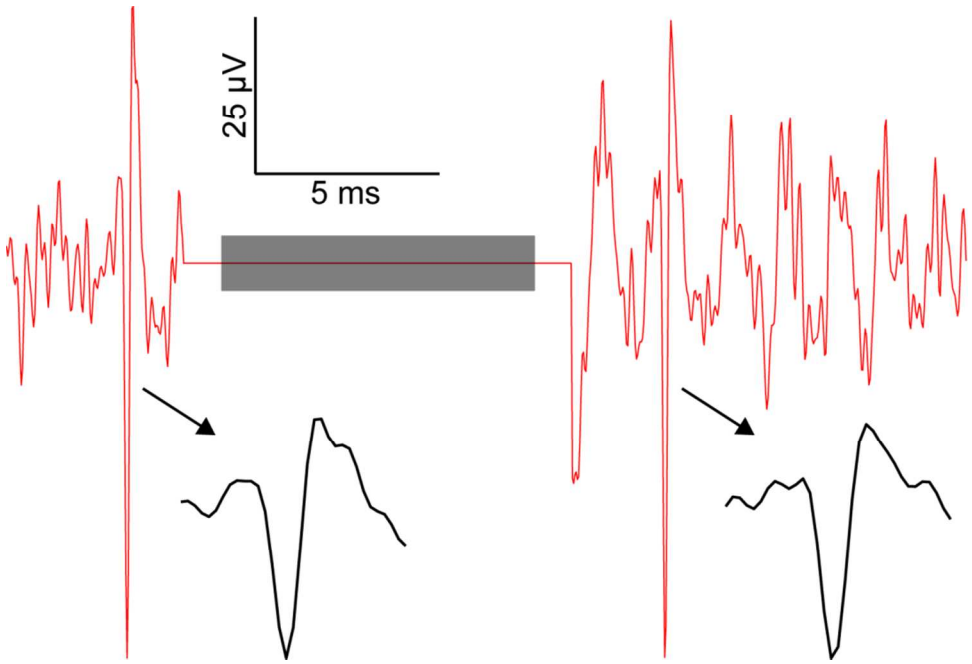


**Figure S-4.** Rapid action potential recovery. Representative electrophysiological trace (band-pass filtered 600 - 6000 Hz) collected in the absence of the solid-state-relay array showing an action potential occurring just before and soon after the voltammetric scan (grey box). Insets display expanded view of each waveform illustrating that the shape of the measured action potential is preserved.

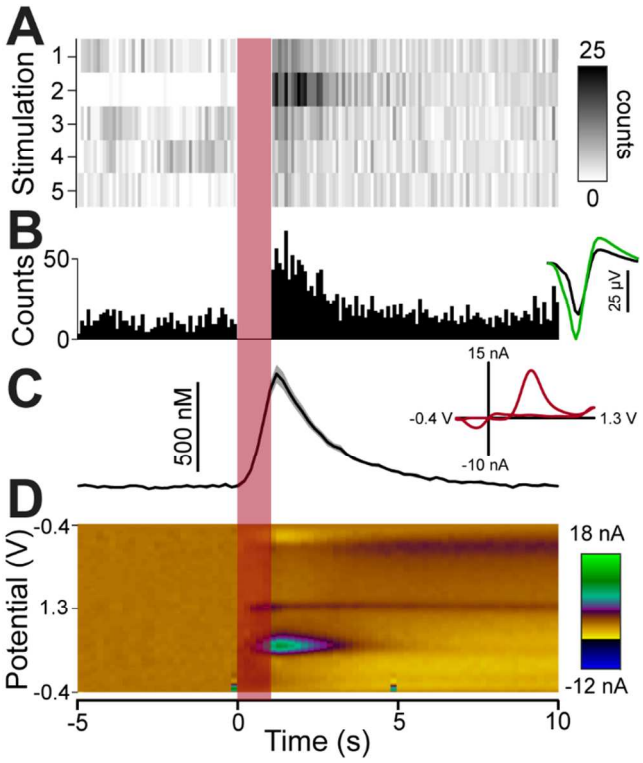


**Figure S-5.** Simultaneous measurement of single-neuron activity and dopamine release with solid-state-relay array (SSR). (A) Raster plots of responses of a single neuron to each medial forebrain bundle (MFB) stimulation (indicated by red bar). Stimulation was delivered 5 times (y-axis). (B) Peri-event histogram (PEH) for the five stimulations (left, bin size = 100 ms) and average waveform of neuron measured at each electrode of the stereotrode. While the PEH appears to show a response, this cell was classified as unresponsive as the apparent response is dominated by a single trial and thus not statistically significant. (C) Average change in dopamine concentration in response to MFB stimulation (± SEM). Inset displays a characteristic dopamine voltammogram. (D) Average color plot of dopamine measurement with time on the x-axis, voltage on the y-axis, and current shown in false color.

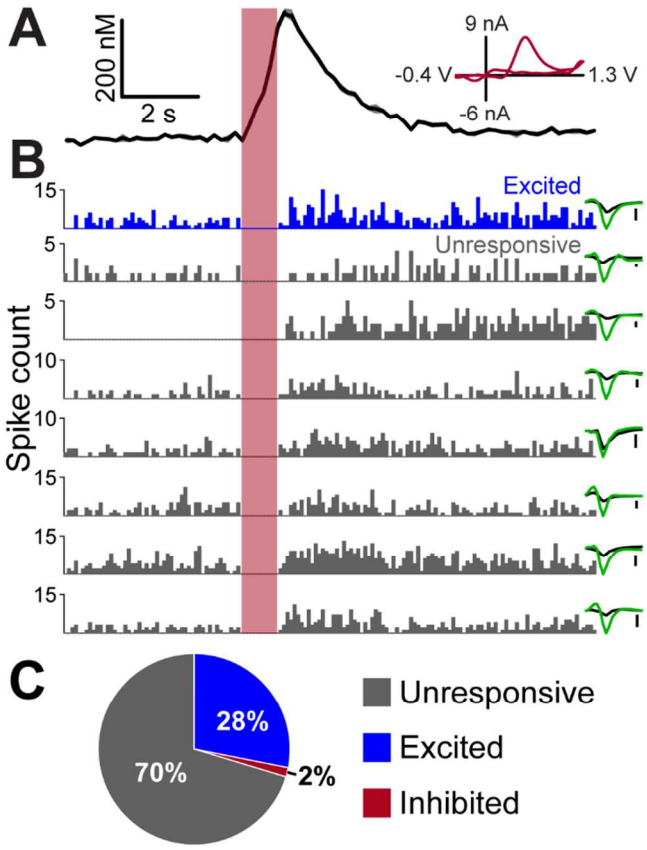


**Figure S-6.** Multiple single-neuron activities in the hippocampus measured with dopamine release in the nucleus accumbens. Recordings were acquired with the solid-state-relay array (SSR). (A) Average evoked dopamine release (n = 5 stimulations, ± SEM). Inset displays characteristic dopamine waveform. (B) Peri-event histograms from eight simultaneously measured hippocampal neurons (bin size = 100 ms). Histograms are color coded for responsiveness as described in C. The waveform of each neuron as measured at the two electrodes of the stereotrode is shown to the right of each histogram. All scale bars are 25 μV. (C) Pie chart showing fraction of all neurons measured using the SSR (n = 3 rats, 64 cells total) with firing rates that were non-responsive, increasing, or decreasing in following MFB stimulation. Responsiveness was determined using paired Student's t-test of the average firing rate five seconds before and after the stimulation (n = 5 stimulations). The percentages of cells measured in each category is similar to that measured without the SSR (74% unresponsive, 21% excited, and 5% inhibited, n = 3 rats, 119 cells).