Active electrode compensation for single-electrode intracellular recordings

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The electrode introduces a bias in the recording when current is injected: $V_r(t) = V_m(t) + U_e(t)$.

Demanding protocols:

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- Electrode \approx resistance: $U_e(t) \approx R_e I(t)$.
- Not an ideal resistance → capacitive transients.
- Fast dynamic clamp is impossible (oscillatory instability).
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Discontinuous current clamp (DCC)



sampling (1.5-3 kHz)

• Current injection and voltage recording are alternated.

- No capacitive transient but recordings are noisy.
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- Hypothesis: electrode = arbitrary linear filter with kernel $K_e(t)$.
- Electrode response: $U_e(t) = \int_0^{+\infty} K_e(s) I(t-s) ds$.
- Calibrate the electrode model K_e, then compensate the recording: V_m = V_r K_e * I

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Finding the electrode kernel K_e



- The kernel must be estimated intracellularly.
- Estimate the full kernel of the system neuron + electrode + amplifier.
- Remove the neuron contribution.

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Electrode kernels



• The kernel changes after impalement.

- Kernels have three phases: 1) feedback delay, 2) fast rising phase, 3) slower decay.
- The kernel also captures the characteristics of the amplifier (filters, capacitance neutralization).

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Dynamic clamp Conductance waves



• AEC recordings are more precise.

• AEC recordings agree with theoretical predictions.

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- Excitatory and inhibitory conductances mimicking synaptic activity *in vivo* can be injected with DCC, but the recording quality is limited.
- Spikes are recorded with high resolution with AEC.

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Dynamic clamp Synaptic noise



• Precise temporal features can be recorded with AEC.

• The slope-threshold relationship is present in AEC recordings only.

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White noise injection



- The response to unfiltered white noise can be recorded with AEC (current-clamp).
- Recordings match theoretical predictions (low noise).

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White noise injection Double-electrode test (patch electrodes)

Badel, Lefort, Brette, Petersen, Gerstner and Richardson. J Neurophysiol 99: 656-666 (2008).



- Double-electrode recordings show that white noise injection also degrades recordings with low-resistance electrodes (whole-cell patch clamp).
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- The membrane capacitance and the I-V curve are measured from the response to white noise.

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- Electrode properties are stable over time.

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AEC in vivo



- The electrode kernel can be estimated during spiking activity.
- AEC compensation works in vivo (above: white noise).



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- Synaptic conductances can be injected *in vivo* (dynamic clamp) during spontaneous activity.
- Spike timing reliability can be assessed in realistic conditions.

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- Voltage-clamp (in progress, with José Gomez)
- Dendritic recordings
- Measurement of excitatory and inhibitory synaptic conductances

Code online:

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