# DENs of Purkinje Cells

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**Abstract**

In this note, the author provides a surprising path to potentially validating the ephaptic coupling model presented in the author's doctoral dissertation and showing its predictive potential.

Ephaptic coupling represents a non-synaptic mechanism whereby neurons communicate through extracellular electric fields generated by their own activity. In the work by Chawla and Morgera [1], differential ephaptic networks emerge from relaxing the assumption of electroneutrality in axon tracts, allowing for signed interactions that modulate action potential timing. This relaxation is justified by empirical data on nerve boundary conductivities, which are not perfectly insulating but rather semiconductor-like, permitting current leakage across the tract. Consequently, the geometric W-matrix incorporates negative entries, leading to delays in action potential initiation that mimic inhibitory effects, akin to inhibitory postsynaptic potentials delaying firing at synapses. Such signed couplings enhance the nervous system's capacity for signal processing, potentially replicating synapse-like information transmission without neurotransmitters. In contrast, Han and colleagues [2] demonstrate that ephaptic coupling drives sub-millisecond synchronous firing among neighboring Purkinje cells in the cerebellar cortex of awake mice. Their recordings reveal that most nearby Purkinje cells exhibit correlated spiking with a characteristic zero-latency dip and peaks at plus or minus 0.5 milliseconds, persisting even when chemical and electrical synapses are blocked. This synchrony arises from extracellular potentials produced by one Purkinje cell's action potential rapidly depolarizing the axon initial segment of adjacent cells, activating sodium channels to trigger firing. The mechanism relies on the highly localized negative extracellular signals peaking during the action potential's rising phase, with efficacy dictated by the proximity of axon initial segments, typically within tens of micrometers. Integrating these findings, the differential framework from Chawla and Morgera can extend to Purkinje cell interactions, where the cerebellar environment may not enforce strict electroneutrality due to finite conductivities in surrounding tissues like the granular layer and molecular layer glia. In Purkinje cell axon bundles descending toward the white matter, leakage could introduce negative contributions to the effective coupling matrix, transforming purely excitatory ephaptic influences into a mix of excitatory and inhibitory-like effects. This

would manifest as timing shifts in the observed synchrony, with some pairs experiencing delays of 0.5 to 1 millisecond, altering the precise sub-millisecond coordination seen in Han's experiments. For instance, inverting specific matrix entries, as simulated in Chawla and Morgera's three-axon model, shifts voltage traces leftward, delaying initiation in follower axons and potentially explaining the post-synchrony suppression at 1 to 3 milliseconds in cross-correlograms. Such differential ephaptic networks among Purkinje cells could enable more nuanced modulation of cerebellar output, where synchronous volleys to deep nuclei are fine-tuned by variable delays, enhancing error correction and motor learning. The bidirectional yet asymmetric nature of Purkinje cell coupling, dependent on initial segment geometry, aligns with the possibility of unidirectional influences if leakage asymmetrically affects field polarity. Furthermore, cascading ephaptic interactions—Purkinje cell one to ephapse to Purkinje cell two—could form black-box networks replicating synaptic chains, as envisioned by Chawla and Morgera, but devoid of chemical transmission. This perspective suggests that targeting ephaptic mechanisms, alongside synapses, could improve interventions for cerebellar disorders like ataxia, where desynchrony disrupts timing. Applying information-theoretic models, such as Kramer's discrete memoryless channel network, to these differential setups may reveal increased capacity over unsigned cases, supporting richer neural computation in the cerebellum. Overall, relaxing electroneutrality bridges the modeling insights of axon tracts to empirical observations in Purkinje cells, proposing that ephaptic coupling is not merely synchronizing but differentially sculpting temporal patterns for advanced information processing.

## References and Bibliography


[1] A. Chawla and S. Morgera. Differential ephaptic networks. *Journal of Applied Mathematics and Physics*, 10:2876–2882, 2022.

[2] K.-S. Han, C. Guo, C. H. Chen, L. Witter, T. Osorno, and W. G. Regehr. Ephaptic coupling promotes synchronous firing of cerebellar purkinje cells. *Neuron*, 100(3):564–578.e3, 2018.