

Online Resource 6

Neuronal-input and coupling sensitivity

Article

The Syncytial Mesh Model: glial spatial control, neuronal response geometry, and the limits of local EEG reduction

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Contents

Retrospective tests of the spatial transport response under matched input routes and neuronal lateral coupling.

S6 Text. Neuronal-source and lateral-coupling robustness of the seven-domain SMM-K prediction

Status and provenance. These calculations were carried out after examination of the 2026 EEG results. They are retrospective sensitivity analyses of the specified 56-dimensional linear system, not preregistered human experiments, raw EEG reanalyses, nonlinear FEniCS replications or demonstrations of glial causal control in tissue. The code and machine-readable output are supplied as Online Resource 3.

1. Source model and perturbations

Seven identical nodes represent local QIF neuronal/ionic systems, each carrying state $q_i = (r_{E,i}, v_{E,i}, r_{I,i}, v_{I,i}, s_{EI,i}, s_{IE,i}, k_i, a_i)$. The local 8×8 Jacobian A_8 is transcribed from the frozen local EEG realization. A seven-node path Laplacian L has open ends; the spacing is $h = 150 \mu\text{m}$. The extracellular diffusion coefficient is $D_e = 9.55343 \times 10^{-10} \text{ m}^2/\text{s}$ and the reference glial coefficient is $D_g = 3.71479 \times 10^{-10} \text{ m}^2/\text{s}$. The tested model is

$$\dot{q} = (I_7 \otimes A_8 - L \otimes \Gamma) q + b(t), \quad \Gamma = \frac{D_e}{\phi_e h^2} E_{kk} + \frac{D_g}{\phi_a h^2} E_{aa} + \gamma_N E_{r_E r_E}.$$

The first two terms preserve the original potassium operators. The last term is a *new*, phenomenological nearest-neighbour rate-coupling sensitivity parameter and is not an estimate of real synaptic connectivity. The two transport conditions are $D_g = 0$ and $D_g = D_g^{\text{ref}}$ with every other parameter identical. A separate alternative adds a neuronal rate-difference term to excitatory voltage, $\dot{v}_{E,i} \mapsto \dot{v}_{E,i} - (\gamma_V/\tau_E)(Lr_E)_i$, rather than to $\dot{r}_E$. This alternative is not combined with the rate-diffusion change.

Three constant focal inputs are considered independently at the center patch $i = 3$ (indexing from zero): an original idealized astroglial source $b_a = e_i \otimes (e_a/\phi_a)$; an extracellular potassium source attributed phenomenologically to localized neuronal K release, $b_K = e_i \otimes (e_k/\phi_e)$; and direct excitatory neuronal voltage forcing, $b_N = e_i \otimes (e_{v_E}/\tau_E)$. The last input recruits the neuronal-to-potassium source coupling already in A_8 , including the local $J_{RE} r_E/\phi_e$ term, rather than externally injecting potassium. These different source normalizations **are not matched biological doses**; source-to-source amplitudes must not be compared. The within-source D_g response contrast is meaningful because source magnitude is held fixed for each pair.

2. Exact response and checking

For each common spatial mode of the shared path, the model reduces to an 8×8 linear system with Laplacian eigenvalue λ_j . Its exact constant-step response at time t is $q_j(t) = A_j^{-1}(e^{A_j t} - I)b_j$. The modal solution was checked against the explicit 56×56 matrix-exponential calculation: the largest componentwise discrepancy in the reference 20-s condition was 1.688e-13 in the source's numerical units. All eigenvalues retained negative real part in the reported sweep. Neuronal-rate response was examined at 3, 8 and 20 s; the main text reports the 20-s values. The uniform-input solution is transport-invariant within machine precision owing to $L\mathbf{1} = 0$ and homogeneous patches. Numerical identity is **not** an experimental claim that real bath application is exactly spatially uniform.

3. Exact model-level results

The adjacent-to-central excitatory-rate response ratio is $\mathcal{R} = r_E(\text{adjacent})/r_E(\text{center})$. The table reports the 20-s ratios for a representative neuronal lateral-coupling sweep; coefficients for γ_N are in s^{-1} . Values are rounded for display; exact entries, center/neighbor responses, eigenvalue maxima, numerical errors and time sweeps are in `results/neuronal_input_and_lateral_robustness.json`.

Input location / mechanism	γ_N (s^{-1})	$\mathcal{R}$ at $D_g = 0$	$\mathcal{R}$ at reference D_g	Absolute ratio difference
Astroglial drive	0	0.116273	0.256265	0.139992
Astroglial drive	10	0.131594	0.270634	0.139039
Astroglial drive	30	0.159471	0.296626	0.137155
Neuron-derived K source	0	0.118006	0.228659	0.110653
Neuron-derived K source	10	0.133321	0.243351	0.110030

Input location / mechanism	γ_N (s ⁻¹)	$\mathcal{R}$ at $D_g = 0$	$\mathcal{R}$ at reference D_g	Absolute ratio difference
Neuron-derived K source	30	0.161186	0.269957	0.108771
Direct neuronal voltage drive	0	0.000567	0.000876	0.000309
Direct neuronal voltage drive	10	0.016153	0.016442	0.000289
Direct neuronal voltage drive	30	0.044657	0.044913	0.000256

The neuron-derived K-source response gives an adjacent/central ratio of 0.118006 without glial transport and 0.228659 with reference transport in the original uncoupled case. At $\gamma_N = 10$ the same pair becomes 0.133321 versus 0.243351; at $\gamma_N = 30$ it is 0.161186 versus 0.269957. Thus lateral neuronal coupling changes baseline spatial spread, but **does not eliminate** the substantial transport-dependent redistribution for focal neuron-derived K release under the stated matched parameter changes. The direct neuronal voltage drive retains a nonzero but much less salient spatial ratio effect at higher neuronal coupling: at $\gamma_N = 10$, Δr_E is -0.00059515 at the center and $+0.00017575$ adjacent, compared with an approximately 0.642 source-normalized central excitatory response. At $\gamma_N = 30$, direct neuronal excitation changes the adjacent response by $+0.00013186$, only **0.49%** of the corresponding no-transport adjacent response. A nonzero response in exact linear arithmetic does not guarantee tissue-level detectability. The transport contrast is therefore sharply input-route-dependent and should not be described as equally robust across neuronal K-source and direct-voltage drives. The alternative neuronal-rate-to-voltage coupling also preserved the sign of the transport contrast in the finite set of stable tested models, and its detailed numerical values are in the JSON.

For an intervention interaction, let $Y_j(t | u, g)$ denote baseline-corrected neuronal response at location j to forcing pattern u and glial condition g . Define $\mathcal{J}_j(t) = [Y_j(t | u_F, g_+) - Y_j(t | u_F, g_-)] - [Y_j(t | u_U, g_+) - Y_j(t | u_U, g_-)]$. In the homogeneous seven-patch model with exactly uniform forcing, the second bracket vanishes numerically; thus $\mathcal{J}_{\text{adjacent}}$ reduces to Δ_{adjacent} in the archived JSON. It is **not** an independently replicated effect. The ratio $\mathcal{R}$ is descriptive rather than the primary prospective observable.

Focal input	γ_N (s ⁻¹)	Neighbor response without glial transport	Adjacent interaction $\mathcal{J}_{\text{adjacent}}$	Interaction / no-transport neighbor (%)
Neuron-derived K source	0	0.00321876	+0.00175077	54.39
Neuron-derived K source	10	0.00353785	+0.00162541	45.94
Neuron-derived K source	30	0.00406722	+0.00141396	34.76
Direct neuronal voltage drive	0	0.00037510	+0.00020404	54.40
Direct neuronal voltage drive	10	0.01036431	+0.00017574	1.70
Direct neuronal voltage drive	30	0.02706388	+0.00013186	0.49

The table uses the frozen source conventions with within-input glial transport on/off comparisons. Input routes are **not calibrated to the same dose**. The ratio becomes relatively insensitive under direct neuronal excitation because neuronal lateral propagation raises its background spatial spread; therefore the modest surviving direct-drive interaction cannot establish experimental discriminability by itself. S1 Fig displays the focal neuron-derived K response, the neighbor interaction across neuronal coupling, and the descriptive ratios; all are conditional model predictions, not confidence intervals.

4. What this result does and does not discriminate

At fixed neuronal coupling, glial transport changes the simulated spatial response for both neuron-derived potassium input and direct neuronal excitation. The magnitude of this effect depends strongly on the input route.

These results do not establish that a flexible neuronal-only spatial model could never reproduce the response after retuning its own coupling strengths. To distinguish mechanisms experimentally, use $\mathcal{I}_j(t)$ as a prospective **stimulus-pattern by glial-coupling interaction** under shared baseline physiology and with direct extracellular-potassium and astrocytic-state measurements, specifying a minimum resolvable effect before data collection. Quantify the change in spatial response under both focal and verified approximately homogeneous perturbations; compare predictive models with neuronal coupling constrained by independent recordings. These conditions block a superficial post hoc explanation but do not assume pharmacological or genetic specificity.

Historical experimentation on astroglial spatial buffering provides the relevant precedent: Orkand et al. (1966), Kofuji and Newman (2004), Wallraff et al. (2006), and Pannasch et al. (2011), as cited in the main manuscript. However, Cx30/Cx43 manipulations also affect glutamate clearance, extracellular-space volume and neuronal excitability, and Wallraff et al. document that some potassium clearance persists without coupling. A simple two-group difference thus does **not** identify the scalar D_g without additional biological constraints.

5. Reproducibility and epistemic boundary

Programs: `code/neuronal_input_coupling_robustness.py` and `code/plot_reviewer_robustness.py` in S3 Data and Code. Exact JSON: `results/neuronal_input_and_lateral_robustness.json`. The frozen source matrix is unchanged and included as `code/audit_frozen_eeg_m3_local.py`; its provenance is separately documented. Command: `python code/neuronal_input_coupling_robustness.py` from an extracted S3 archive, followed by `python code/plot_reviewer_robustness.py`. The scripts assert stability, uniform cancellation and modal/full-matrix agreement. Nothing in this post-outcome computation modifies the participant-level EEG scores or the historical *NOT EVALUABLE* and *POST_OPEN_AMENDED* classifications.