Thalamo-Cortical Neural Mass Model with 5-HT$_{2A}$ Modulation & Explanation of the Linearisation and Transfer Function Equations

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Model Equations

The following equations define a conductance-based thalamo-cortical neural mass model with serotonergic (5-HT$_{2A}$) modulation. The model describes how membrane potentials, synaptic conductances, and neuromodulatory effects evolve over time, and how they can be expressed in both time and frequency domains.

Let [5-HT] denote the local serotonin concentration and $s = \exp(P_s)$ be a serotonin gain parameter (where P_s is a log-parameter controlling scaling).

1. Membrane Dynamics

$$C\frac{dV}{dt} = \sum_k g_k(V_k - V) + g_{\text{NMDA}} \cdot f_{\text{MG}}(V) \cdot (V_{\text{NMDA}} - V) + u \tag{1}$$

This is the standard current-balance equation: the change of membrane potential V over time depends on the capacitive current ($C\,dV/dt$) and the sum of ionic currents. Each conductance g_k drives the potential towards its reversal potential V_k. The NMDA current has an additional nonlinearity, $f_{\text{MG}}(V)$, that reflects magnesium block. u represents any external input (e.g., sensory drive or stimulation).

2. Conductance Dynamics

$$\dot{g}_k = \kappa_k\,(\varsigma_k - g_k) + \Gamma_g \tag{2}$$

The conductances themselves are dynamical: they relax towards a target value ς_k at a rate κ_k, with additional baseline or noise terms Γ_g.

Here k indexes the specific receptor or ion channel types: {AMPA, NMDA, GABA$_A$, GABA$_B$, M-type K^+, HCN, 5-HT$_{2A}$}.

$$\varsigma_k = H \cdot \text{firing} + \text{BE} \tag{3}$$

The target conductance ς_k is a function of presynaptic firing (scaled by a gain H) plus a baseline/extrinsic drive (BE).

3. NMDA Magnesium Block

$$f_{\mathrm{MG}}(V) = \frac{1}{1 + 0.2 \cdot \exp(-\alpha_{\mathrm{NMDA}} V)} \tag{4}$$

This function captures the voltage-dependent magnesium block of NMDA receptors: at hyperpolarised potentials, magnesium ions occlude the channel, while depolarisation relieves the block.

5-HT$_{2A}$ Modulation of Conductances

Serotonin acts as a neuromodulator by multiplicatively scaling synaptic and channel conductances. This allows the model to capture how 5-HT$_{2A}$ receptor activation alters excitatory–inhibitory balance and intrinsic excitability.

$$g_{\mathrm{NMDA}}^{\text{5-HT}} = g_{\mathrm{NMDA}} \cdot (1 + 0.2 \cdot s \cdot [\text{5-HT}]) \tag{5}$$
$$g_{\mathrm{GABA}_A}^{\text{5-HT}} = g_{\mathrm{GABA}_A} \cdot (1 - 0.2 \cdot s \cdot [\text{5-HT}]) \tag{6}$$
$$g_{\mathrm{GABA}_B}^{\text{5-HT}} = g_{\mathrm{GABA}_B} \cdot (1 + 0.1 \cdot s \cdot [\text{5-HT}]) \tag{7}$$
$$g_{\mathrm{M}}^{\text{5-HT}} = g_{\mathrm{M}} \cdot (1 - 0.2 \cdot s \cdot [\text{5-HT}]) \tag{8}$$
$$g_{\mathrm{HCN}}^{\text{5-HT}} = g_{\mathrm{HCN}} \cdot (1 + 0.1 \cdot s \cdot [\text{5-HT}]) \tag{9}$$

Here serotonin enhances NMDA and HCN conductances, reduces GABA$_{\mathrm{A}}$ and M-type currents, and slightly enhances GABA$_{\mathrm{B}}$. This captures experimentally observed effects of psychedelics and serotoninergic drugs: promoting excitation, increasing dendritic currents, and altering oscillatory dynamics.

Linearisation and Transfer Functions

We treat the full system of equations above as a nonlinear dynamical system:

$$\frac{dx}{dt} = f(x, u, P, M) \tag{10}$$
$$y = g(x, P) \tag{11}$$

where x are state variables (e.g., voltages, conductances), u are inputs, P are parameters, and M defines the model structure. Outputs y correspond to measured signals (EEG/MEG).

Linearisation Around a Fixed Point

Nonlinear dynamics can be approximated by linear dynamics in the neighbourhood of a steady state (x_0, u_0):

$$\frac{dx}{dt} \approx Ax + Bu \tag{12}$$
$$y \approx Cx \quad [+\, Du \text{ if present}] \tag{13}$$

Here:

- $A = \left.\frac{\partial f}{\partial x}\right|_{x_0,u_0}$: Jacobian of the system; captures local stability and oscillatory tendencies.
- $B = \left.\frac{\partial f}{\partial u}\right|_{x_0,u_0}$: how inputs perturb the states.
- $C = \left.\frac{\partial g}{\partial x}\right|_{x_0}$: mapping from hidden states to observed signals.

This linearisation makes it possible to use spectral (frequency-domain) methods, since linear systems have well-defined transfer functions.

Laplace-Domain Transfer Function

Applying the Laplace transform:

$$Y(s) = C(sI - A)^{-1}BU(s) + C(sI - A)^{-1}x_0 \tag{14}$$

This compact equation expresses how inputs $U(s)$ and initial states x_0 produce outputs $Y(s)$ at frequency s.

Explanation of Terms

- $Y(s)$: Output (e.g., EEG/MEG spectra).
- $U(s)$: Input (sensory or stimulation signals).
- A: Internal coupling dynamics; eigenvalues determine oscillatory modes and stability.
- B: Pathways by which inputs drive the neural states.
- C: Mapping from internal neural states to observed signals.
- x_0: Initial state of the system.
- $(sI - A)^{-1}$: The resolvent, describing how dynamics filter and shape responses across frequencies.

Interpretation in Neuroscience

- $C(sI - A)^{-1}BU(s)$: *Stimulus-driven response* - how external perturbations (e.g., stimuli, TMS) are filtered by network dynamics.
- $C(sI - A)^{-1}x_0$: *Spontaneous response* - how intrinsic fluctuations generate rhythms or oscillations, even without inputs.

In practice, this linearised frequency-domain formulation underpins Dynamic Causal Modelling (DCM): allowing one to fit empirical EEG/MEG spectra and infer parameters such as synaptic strengths, neuromodulator effects, and system stability.