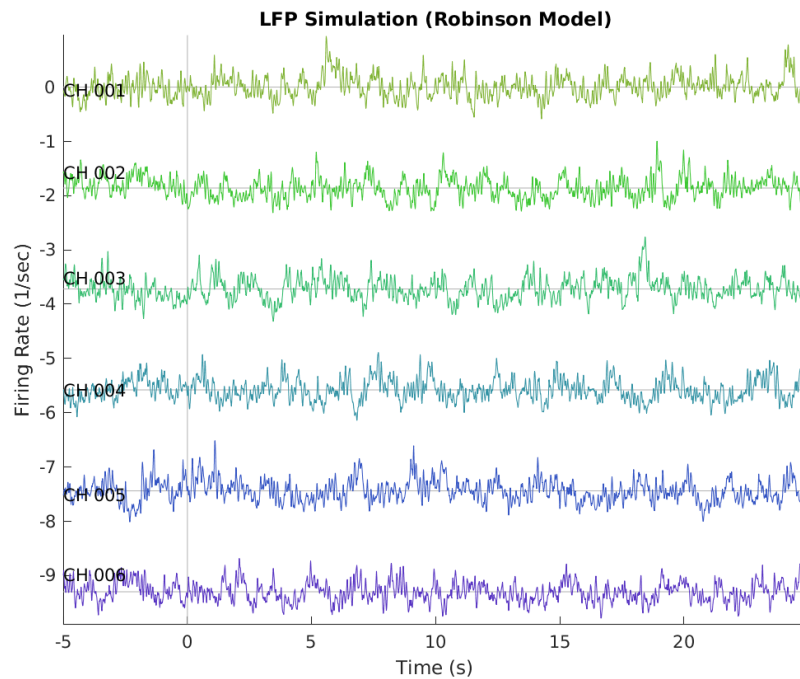


# NeuroLoop Utilities – Model-Based Synthesis Guide

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# Chapter 1

## Overview

This document describes the models used for synthesizing proxy neural activity using the “**nlSynth\_**” family of library functions.

These functions are primarily intended to produce realistic-looking signals with known qualities to test analysis scripts with. That said, these models are drawn from publications where they were used to provide insight into the functioning of brain networks, so using these functions for such research is an additional use-case.

Chapter 2 describes the neural model presented in Robinson 2002 (and elaborated on in Freyer 2011 and Hindriks 2023). This is a model of average firing rates of multiple neural populations in the cortex and thalamus, with feedback connections that drive noise-excited oscillations.

**FIXME: Other models go here once they’re added.**

# Chapter 2

## Robinson Model

The model presented in Robinson 2002 (hereafter “the Robinson model”) provides a series of differential equations relating the firing rates of multiple neural populations in the cortex and thalamus. Feedback between these regions drives noise-excited oscillations.

The most relevant references are:

- Robinson 2002 – Describes the model, finds steady-state points, and analyzes perturbations around those points to find oscillation modes.
- Freyer 2011 – Describes an extension to the model where noise is modulated by the network’s own output, providing a closer match to the distribution of oscillation modes in biological data.
- Hindriks 2023 – Describes an extension to the model that adds multiple independent copies of the Robinson and Freyer model, with coupling between instances. This is used to model co-oscillation of different brain regions in biological data.

(See Section 2.2 for citations.)

### 2.1 Model Description

A diagram of the Robinson model with the extensions from Freyer 2011 and Hindriks 2023 is shown in Figure 2.1. To distinguish this from the Robinson 2002 model, this will be referred to as “the extended Robinson model”.

The neural population model is described in Equations 2.1, 2.2 and 2.3. Per Equation 2.1, a weighted sum of input firing rates  $\phi_b(t)$  is used to generate the cell body potential  $V_a(t)$ . A single dot indicates the first time derivative, and a double dot indicates the second time derivative. The parameters  $\alpha$  and  $\beta$  are the inverse of the membrane potential fall time and rise time, respectively. The coupling parameter  $\nu_{ab}$  is the strength of the connection from region  $b$  to region  $a$  (zero if no connection, negative if inhibitory).

**NOTE:** A delay is manually applied to some of the  $\phi_b$  signals before this summation to reflect signal propagation time between the cortex and thalamus (per Robinson 2002), and to reflect cross-coupling

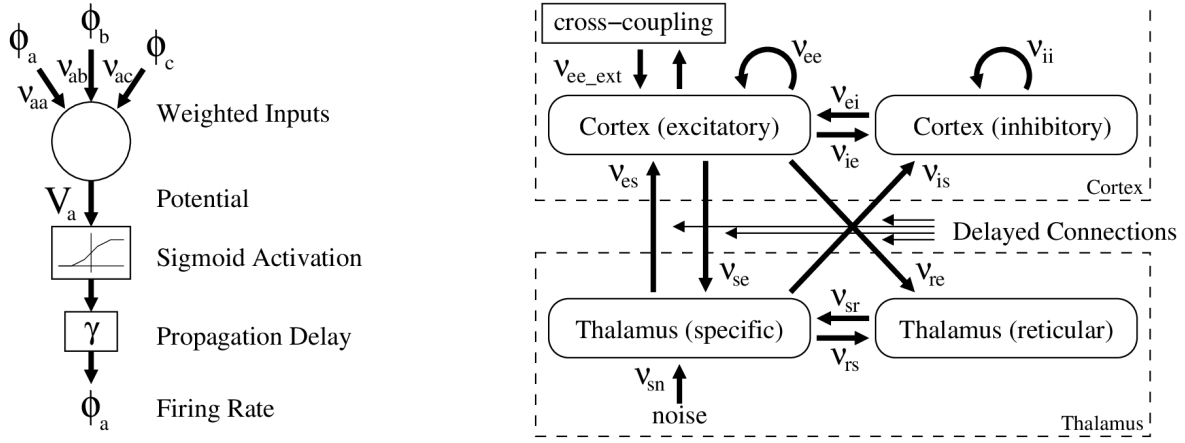


Figure 2.1: Extended Robinson model diagram, showing the neuron population model (left) and the population interactions (right).

delays within the cortex populations (per Hindriks 2023).

$$\left(\frac{1}{\alpha\beta}\right)\ddot{V}_a(t) + \left(\frac{1}{\alpha} + \frac{1}{\beta}\right)\dot{V}_a(t) + V_a(t) = \sum_b \nu_{ab}\phi_b(t) \quad (2.1)$$

Per Equation 2.2, the cell body potential  $V$  is fed into a sigmoid activation function, to represent the collective action of many neurons with varying firing thresholds. The mean firing threshold is  $V_{th}$  and the standard deviation of the threshold is  $\sigma_{th}$ . This follows the convention of Freyer 2011; Robinson 2002 defined a related parameter  $\sigma'_{th} = \frac{\sqrt{3}}{\pi}\sigma_{th}$  to simplify the activation equation.

$$Q(V) = \frac{Q_{max}}{1 + e^{-\left(\frac{\pi}{\sqrt{3}}\right)\left(\frac{V-V_{th}}{\sigma_{th}}\right)}} \quad (2.2)$$

Per Equation 2.3, the local firing rate  $Q$  is propagated with damping and finite delay to give the non-local firing rate  $\phi$ . A single dot indicates the first time derivative, and a double dot indicates the second time derivative. Per Robinson 2002, local propagation delay is assumed to only be relevant within the cortex, and  $\gamma = \infty$  is assumed elsewhere. Per Freyer 2011, this further only applies to the excitatory neuron populations in the cortex.

$$\begin{cases} \frac{1}{\gamma^2}\ddot{\phi}(t) + \frac{2}{\gamma}\dot{\phi}(t) + \phi(t) = Q(t) & \text{Cortex excitatory neurons.} \\ \phi(t) = Q(t) & \text{All other populations.} \end{cases} \quad (2.3)$$

Noise is injected into the model as  $\phi_n$ , and is described by Equation 2.4. Per Freyer 2011, there are three components: constant, additive, and multiplicative. Multiplicative noise (noise modulated by  $\phi_e$ ) is important for broadening the distribution of peak power levels of transient oscillations at frequencies above the fundamental oscillation mode of the cortex/thalamus loop.

In Equation 2.4,  $\phi_n$  is the noise coupled to the thalamus via  $\nu_{sn}$ ,  $\mu_n$  is the constant noise component (background firing rate),  $\sigma_n$  is the standard deviation of the independent component of the noise, and

$\chi$  is a scaling parameter (per Freyer 2011) such that  $\sigma_n\chi$  is the standard deviation of the component of the noise that is modulated by  $\phi_e$ . Since the  $\phi_e$  signal has to propagate from the cortex to the thalamus before modulating this noise component, it is manually delayed. The signals  $g_1(t)$  and  $g_2(t)$  denote two independent Gaussian noise sources with zero mean and with standard deviations of 1.

$$\phi_n(t) = \mu_n + \sigma_n g_1(t) + \sigma_n \chi g_2(t) \phi_e(t - t_{halfloop}) \quad (2.4)$$

As shown in Figure 2.1, cross-coupling between excitatory cortical populations is implemented per Hindriks 2023. This is described by Equation 2.5. Weight values  $w_{ab}$  represent the strength of connections between populations, and delay values  $t_{coupling_{ab}}$  represent the propagation delays of these connections. While arbitrary weight values may be chosen, the recommended implementation is to use positive weights (purely excitatory), with the constraint that the sum of all weights contributing to a given  $\phi_{ext_k}$  should sum to approximately unity. Cross-coupling propagation delay is typically no more than  $\frac{1}{\gamma}$ .

$$\phi_{ext_a}(t) = \sum_b w_{ab} \phi_e(t - t_{coupling_{ab}}) \quad (2.5)$$

$$\forall a, \sum_b w_{ab} \approx 1 \quad (2.6)$$

Typical parameter values for the extended Robinson model are shown in Table 2.1. Typical coupling coefficients are shown in Table 2.2. These are very similar to the parameter and coupling coefficient values used in Hindriks 2023.

Parameter	Value	Units	Notes
$Q_{max}$	250	$\text{sec}^{-1}$	maximum firing rate
$V_{th}$	15	mV	potential threshold for firing
$\sigma_{th}$	6	mV	standard deviation of firing threshold
$\alpha$	50	$\text{sec}^{-1}$	membrane potential inverse fall time
$\beta$	200	$\text{sec}^{-1}$	membrane potential inverse rise time
$\gamma$	100	$\text{sec}^{-1}$	cortex inverse propagation delay
$t_{halfloop}$	40	ms	one-way cortex/thalamus delay
$\mu_n$	0	$\text{sec}^{-1}$	constant noise firing rate
$\sigma_n$	0.1	$\text{sec}^{-1}$	additive noise standard deviation
$\chi$	0.3	dimensionless	multiplicative noise deviation coefficient

Table 2.1: Typical parameters for the extended Robinson model.

Robinson 2002 describes several oscillating modes: slow-wave/delta-wave oscillation, theta/fast delta oscillation with stable frequency (3 Hz) but varying shape, spindle oscillations at about 10 Hz driven by intra-thalamic resonance, and alpha oscillations at about 10 Hz. These are parameterized in terms of the amplification provided by each population of neurons (Equations 13-15 and Figure 3 in that reference).

The parameter values used in Freyer 2011 and Hindriks 2023 were chosen to support biologically relevant oscillations when driven by external noise.

$\nu_{ee}$	1.2
$\nu_{ei}$	-1.8
$\nu_{es}$	1.2
$\nu_{ie}$	1.2
$\nu_{ii}$	-1.8
$\nu_{is}$	1.2
$\nu_{se}$	1.2
$\nu_{re}$	0.4
$\nu_{sr}$	-0.8
$\nu_{rs}$	0.2
$\nu_{sn}$	0.5
$\nu_{ee_{ext}}$	0.07

Table 2.2: Typical coupling coefficient values for the extended Robinson model.

## 2.2 References

- P. A. Robinson, C. J. Rennie, and D. L. Rowe, *Dynamics of Large-Scale Brain Activity in Normal Arousal States and Epileptic Seizures*, Physical Review E, 65, 041924, April 2002
- F. Freyer, J. A. Roberts, R. Becker, P. A. Robinson, P. Ritter, and M. Breakspear, *Biophysical Mechanisms of Multistability in Resting-State Cortical Rhythms*, Journal of Neuroscience, 31, pp 6353–6361, April 2011
- R. Hindriks and P. K. B. Tewarie, *Dissociation Between Phase and Power Correlation Networks in the Human Brain is Driven by Co-Occurrent Bursts*, Communications Biology, 6, 286, March 2023

## 2.3 Model Analysis

### 2.3.1 Low-Pass Filter Delays

Applying the Laplace transform to Equation 2.1 shows that the effect of  $\alpha$  and  $\beta$  is to apply a low-pass filter to the weighted sum of input firing rates (a second-order exponential smoothing filter with poles at  $-\alpha$  and  $-\beta$ ).

$$\left(\frac{1}{\alpha\beta}\right)s^2V_a(s) + \left(\frac{1}{\alpha} + \frac{1}{\beta}\right)sV_a(s) + V_a(s) = \sum_b \nu_{ab}\Phi_b(s) \quad (2.7)$$

$$s^2V_a(s) + (\alpha + \beta)sV_a(s) + \alpha\beta V_a(s) = \alpha\beta \sum_b \nu_{ab}\Phi_b(s) \quad (2.8)$$

$$(s + \alpha)(s + \beta)V_a(s) = \alpha\beta \sum_b \nu_{ab}\Phi_b(s) \quad (2.9)$$

$$\frac{V_a(s)}{\sum_b \nu_{ab}\Phi_b(s)} = \frac{\alpha\beta}{(s + \alpha)(s + \beta)} \quad (2.10)$$

Applying the Laplace transform to Equation 2.3 shows that the effect of  $\gamma$  is to apply a low-pass filter to the firing rate (a second-order exponential smoothing filter with both poles at  $-\gamma$ ).

$$\left(\frac{1}{\gamma^2}\right) s^2 \Phi(s) + \left(\frac{2}{\gamma}\right) s \Phi(s) + \Phi(s) = Q(s) \quad (2.11)$$

$$s^2 \Phi(s) + 2\gamma s \Phi(s) + \gamma^2 \Phi(s) = \gamma^2 Q(s) \quad (2.12)$$

$$(s + \gamma)^2 \Phi(s) = \gamma^2 Q(s) \quad (2.13)$$

$$\frac{\Phi(s)}{Q(s)} = \frac{\gamma^2}{(s + \gamma)^2} \quad (2.14)$$

The effect of both of these filters is to suppress high-frequency oscillations (those above the filter corner frequencies) and to delay low-frequency oscillations by an amount approximately equal to the filters' time constants. These delays and corner frequencies are listed in Table 2.3 (using the parameter values from 2.1).

Parameter	Value	Corner	Delay
$\alpha$	50 sec <sup>-1</sup>	8 Hz	20 ms
$\beta$	200 sec <sup>-1</sup>	32 Hz	5 ms
$\gamma$	100 sec <sup>-1</sup>	16 Hz	20 ms*

\*Each pole at  $-\gamma$  introduces a 10 ms delay; there are two such poles.

Table 2.3: Robinson model low-pass filter corners and low-frequency delays.

### 2.3.2 Oscillation Modes and Oscillation Criteria

A simplified diagram of the extended Robinson model is shown in Figure 2.2. This is intended to make it easy to identify the feedback loops that may support oscillations. Blue arcs indicate positive coefficients, and red arcs indicate negative (inhibitory) coefficients. As an approximation, the activity of different excitatory neuron populations within the cortex is assumed to be the same, combining  $\nu_{ee}$  and  $\nu_{ee\_ext}$ . Additionally, multiplicative portion of the noise is treated as a contribution to the  $\nu_{se}$  arc. The average contribution of the  $\chi\sigma_n\nu_n$  term is zero, but the magnitude of that term compared to the magnitude of  $\nu_{se}$  indicates whether or not multiplicative noise significantly contributes to that arc.

A list of potential oscillation loops and their oscillation frequencies is given in Table 2.4. For loops consisting entirely of positive coefficients, the oscillation period is the time needed to complete a single circuit. For loops with one negative coefficient, the oscillation period is the time needed to complete two circuits around the loop (in the same manner as a ring oscillator). Harmonics of these oscillation frequencies are also supported.

The number of arc traversals needed for one oscillation period is noted. Per above, this may reflect either one or two cycles around the loop. Each arc traversal involves gain from arc coefficients (noted in the table), small-signal gain from the  $Q(V)$  transfer function (omitted from the table), and delay from the  $\alpha$  and  $\beta$  filter components. Delay contributions from the cortex excitatory population  $\gamma$  filter component and from the cortex-thalamus loop are noted in the table where applicable.



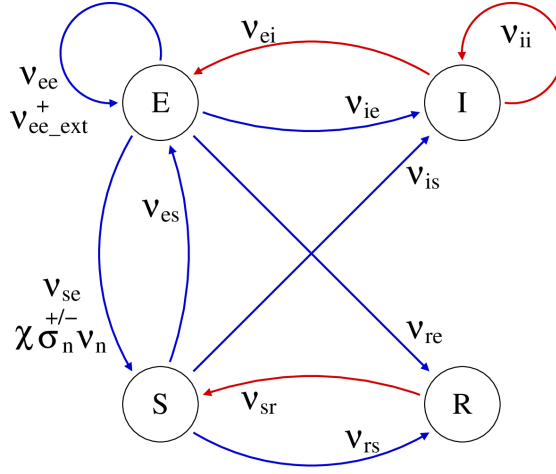


Figure 2.2: Simplified diagram of the extended Robinson model, showing feedback loops.

Label	Arcs	Gamma	C-T Loop	Period	Frequency	Gain
ES	2	Y	Y	150 ms	6.7 Hz	$\nu_{se} \cdot \nu_{es}$
EE	1	Y	–	45 ms	22 Hz	$\nu_{ee} + \nu_{ee\_ext}$
EI	4	Y	–	140 ms	7 Hz	$2 \cdot \nu_{ie} \cdot \nu_{ei}$
SR	4	–	–	100 ms	10 Hz	$2 \cdot \nu_{rs} \cdot \nu_{sr}$
ERS	6	Y	Y	350 ms	2.9 Hz	$2 \cdot \nu_{re} \cdot \nu_{sr} \cdot \nu_{es}$
ESI	6	Y	Y	350 ms	2.9 Hz	$2 \cdot \nu_{se} \cdot \nu_{is} \cdot \nu_{ei}$

Table 2.4: Extended robinson model oscillation modes. Top two modes: single-cycle. Bottom four modes: two-cycle (inverting).

Resonant loops explicitly described in Section IV of Robinson 2002 are the ones marked ES, ERS, and SR. The oscillation periods described in Section V of Robinson 2002 are consistent with the estimated periods of the ERS and SR loops in Table 2.4.

The authors of Robinson 2002 were primarily concerned with noise-excited oscillations, and so only evaluated oscillation loops that included the specific nucleus. Evaluation was expressed in terms of the transfer function from the noise signal (input) to the firing rate of cortex excitatory neurons (output). Resonant oscillations were presumed to occur at frequencies for which this transfer function diverged (producing arbitrarily large output for finite input). This work instead considers gain within a loop, with resonant oscillations corresponding to a loop gain exceeding unity. As this does not explicitly consider noise excitation, all of the loops described in Table 2.4 may be analyzed.

### 2.3.3 Operating Points and Parameter Choices

As was described in Robinson 2002, the dynamics of the extended Robinson model can be analyzed by considering unchanging (DC) firing rates, and evaluating the small-signal gain around these operating points. While this was used to find the transfer function  $\frac{\phi_e(\omega)}{\phi_n(\omega)}$  in Robinson 2002, here it is used to find the small-signal loop gain (to determine which oscillating modes are dominant for given parameter values).

At a given operating point, the sensitivity of the gain of the dominant loops to each of the  $v_{ab}$  coefficients provides insight into which network connections are most relevant for influencing dynamics at that operating point.  $v_{ee\_ext}$  is particularly of interest, as this may be used as a proxy for the sensitivity of network dynamics to changes in the connectivity matrix between different excitatory cortex neuron populations.

For time-independent operating point analysis, Equation 2.1 reduces to:

$$V_a(t) = \sum_b \nu_{ab} \phi_b(t) \quad (2.15)$$

Equation 2.2 is unchanged, and Equation 2.3 reduces to:

$$\phi_a(t) = Q(V_a(t)) \quad (2.16)$$

The gain  $G_{ab}$  of any given arc is the derivative of its output firing rate with respect to its input firing rate. For oscillations with frequencies much lower than the  $\alpha$ ,  $\beta$ , and  $\gamma$  filter corner frequencies, this may be estimated by taking the derivative of the DC operating point equations (rather than requiring an analysis of the full system dynamics):

$$G_{ab} = \frac{d\phi_a}{d\phi_b} = \frac{d}{d\phi_b} [Q(V_a)] \quad (2.17)$$

$$G_{ab} = Q'(V_a) \frac{dV_a}{d\phi_b} \quad (2.18)$$

$$G_{ab} = Q'(V_a) \frac{d}{d\phi_b} \left[ \sum_c \nu_{ac} \phi_c \right] \quad (2.19)$$

$$G_{ab} = Q'(V_a) \nu_{ab} \quad (2.20)$$

The sigmoid response function is defined in terms of the logistic function:

$$\begin{cases} Q(V) = Q_{max} L\left(\frac{V-V_{th}}{\sigma'_{th}}\right) \\ L(x) = \frac{1}{1+e^{-x}} = \frac{e^x}{1+e^x} \\ \sigma'_{th} = \frac{\sqrt{3}}{\pi} \sigma_{th} \end{cases} \quad (2.21)$$

The derivative of the logistic function is:

$$L'(x) = L(x) (1 - L(x)) = \frac{e^x}{(1 + e^x)^2} \quad (2.22)$$

This gives the derivative of the sigmoid response function:

$$Q'(V) = Q_{max} L' \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \frac{d}{dV} \left[ \frac{V - V_{th}}{\sigma'_{th}} \right] \quad (2.23)$$

$$Q'(V) = \frac{Q_{max}}{\sigma'_{th}} L' \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \quad (2.24)$$

$$Q'(V) = \frac{Q_{max}}{\sigma'_{th}} L \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \left( 1 - L \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \right) \quad (2.25)$$

$$Q'(V) = \frac{Q_{max}}{\sigma'_{th}} L \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \left( 1 - \frac{Q_{max}}{Q_{max}} L \left( \frac{V - V_{th}}{\sigma'_{th}} \right) \right) \quad (2.26)$$

$$Q'(V) = \frac{1}{\sigma'_{th}} Q(V) \left( 1 - \frac{Q(V)}{Q_{max}} \right) \quad (2.27)$$

Combining this with Equation 2.20 gives:

$$G_{ab} = \frac{\nu_{ab}}{\sigma'_{th}} Q(V_a) \left( 1 - \frac{Q(V_a)}{Q_{max}} \right) \quad (2.28)$$

$$G_{ab} = \frac{\nu_{ab}}{\sigma'_{th}} \phi_a \left( 1 - \frac{\phi_a}{Q_{max}} \right) \quad (2.29)$$

This is Equation 10 from Robinson 2002. The small-signal gain of a loop at low frequencies is the product of  $G_{ab}$  for each arc in the loop (as with the  $S_d$ ,  $S_i$ , and  $S_r$  values in section IV of Robinson 2002).

**FIXME:** Show how to find operating points. Pick regions of parameter space from Robinson and also note where Hindriks' parameters were in that space. Evaluate loop gains at these locations and their sensitivity to weights. Add an area sensitive to mixing matrix weights if we don't already have one.