Analysis of bursting dynamics in a modified facilitation-depression model accounting for afterhyperpolarization

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Abstract

The activity of neuronal networks can exhibit periods of bursting, the properties of which remain unclear. To study the bursting dynamics of a network, we develop a new stochastic model based on synaptic properties that also accounts for afterhyperpolarization, which shapes the end of a burst. A stochastic perturbation of this system leads to a succession of bursts and interbursts and we characterize their durations using a three dimensional phase-space analysis and numerical simulations. The phase-space contains three critical points (one attractor and two saddles) separated by a two-dimensional stable manifold Σ. Bursting is defined by long deterministic excursions outside the basin of attraction, while the interburst duration is defined by the escape induced by random fluctuations. To characterize the distribution of the burst durations, we determine the distribution of exit points located on the two-dimensional separatrix Σ. In addition, we compute analytically the mean burst and AHP durations using a linearization approximation of the dynamical system. Finally, we explore how various parameters such as the network connectivity and the afterhyperpolarization characteristics influence bursting and AHP dynamics. To conclude, this new model allows us to better characterize the role of various physiological parameters on bursting dynamics.

Introduction

Electrophysiological recordings of neuronal networks reveal periods of synchronous high-frequency activity called bursts separated by interbursts (quiet time periods). Bursting can either be due to intrinsic channel properties driven by Ca$^{2+}$ and/or voltage-gated channels, or by collective properties of the neuronal network [1]. Several models have been proposed to generate bursting, starting with the classical Wilson-Cowan oscillator, where two reciprocally coupled populations of excitatory and inhibitory neurons exhibit bursting [2,3]. Bursters are modeled as slow-fast dynamical systems using the Hodgkin-Huxley formalism, where the fast dynamics are responsible for the fast spiking and are modulated by the slow variables representing the mean voltage dynamics [4]. The classical Hindmarsh-Rose model [5] implements such strategy with three variables: one for the membrane potential, one for the fast ion channels (fast subsystem) and one for the slow ion channels (slow subsystem). Following this model, different types of bursters have been developed, such as ones with low spike frequency at the beginning and the end of a burst [6]. Similarly, parabolic bursters exhibit fast-oscillation frequencies that vary

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along time with the burst [7]. In periodic bursters, the slow variable, is oscillating periodically, between a set of stable attractors, during these transitions the fast variable exhibits spiking [8]. Bursters can be classified according to their topological bifurcation diagram, where the fast subsystem can lead to two main changes of the state space: 1) resting to spiking, when a stable equilibrium transitions to an attractive limit cycle, 2) spiking to resting for the opposite transition [9,10].

Bursts that emerge as a network property have been studied using different modeling approaches such as coupled integrate and fire neurons [11,12], improved recently by adding noise to connected Hodgkin-Huxley type neurons, to allow desynchronisation [13]. Bursting can also depend on the balance between excitatory and inhibitory neurons: coupling excitatory neurons results in in-phase bursting within the network, whereas inhibitory coupling leads to anti-phase dynamics [14]. Furthermore, time-delays play a crucial role in synchronisation, by generating coherent bursting in the Hindmarsh-Rose model, specifically when the time-delays are inversely proportional to the coupling strength [16].

Central Pattern generators such as the respiratory rhythm in the pre-botzinger complex, mastication or oscillatory motor neurons are involved in the genesis and maintenance of rhythmic patterns. Interestingly, several coupled pacemaker neurons receiving an excitatory input from tonic firing neurons can either lead to bursting, tonic spiking or resting depending on the values of the channel conductances and the neuronal coupling level [20–22].

Rhythm generation based on network bursting also depends on the bursting frequency and the interburst intervals. Synaptic properties shape the genesis and maintenance of bursts [23–25]. Synaptic short-term plasticity modeled in the mean-field approximation, are based on facilitation, depression and network firing rate, leading to a three-dimensional dynamical system. Long interburst intervals have been generated by introducing a double depression model [27]. Interestingly, different levels of facilitation and depression lead to various network dynamics such as resting, bursting or spiking and, when noise is added, up and down state transitions [29]. Such models were used to interpret bursting in small hippocampal neuronal islands to show that the correlation between successive bursts and interbursts could result from synchronous depressing-facilitating synapses. However in all these models, the interburst phase has not attracted much attention. The interburst in hippocampal pyramidal neurons is shaped by various type of potassium and calcium ionic channels, leading to medium and slow hyperpolarizing currents in the cells, a phenomenon known as afterhyperpolarization (AHP). We develop here a facilitation-depression model that accounts for AHP in order to better describe these interburst intervals.

The manuscript is organized as follows: in the first part, we introduce a new dynamical system where we have added the AHP to the facilitation-depression model. We show that this model perturbed by a stochastic noise on the voltage variable can produce bursting periods followed by interburst intervals. We then study the phase-space that reveals three critical points (one attractor and two saddles). To further characterize the distribution of burst durations, we study the distribution of exit points on the stable manifold delimiting the basin of attraction of the stable equilibrium. Finally, we find an analytical formula for the burst and AHP durations. We also study the influence of network connectivity as well as facilitation and depression parameters on burst and interburst using numerical simulations.

1 A generalized facilitation-depression model accounting for AHP

1.1 Model description

We recall here the depression-facilitation short-term synaptic plasticity, a mean-field model for a sufficiently connected ensemble of neurons which consists of a stochastic dynamical system made of three
equations \([26,30]\) for the mean voltage \(h\), the depression \(y\), and the synaptic facilitation \(x\):

\[
\begin{align*}
\tau \dot{h} &= -h + Jx y h^+ + \sqrt{\tau} \sigma \dot{\omega} \\
\dot{x} &= \frac{X - x}{t_f} + K(1 - x) h^+ \\
\dot{y} &= \frac{1 - y}{t_r} - Lx y h^+ ,
\end{align*}
\]  

(1)

The population average firing rate is given by \(h^+ = \max(h, 0)\), which is a linear threshold function of the synaptic current \([29]\). The term \(Jx y\) reflects the combined effect of synaptic short-term dynamics on the network activity. The second equation describes facilitation, while the third one describes depression. The mean number of connections (synapses) per neurons is accounted for by the parameter \(J\) \([35]\). We previously distinguished \([30]\) the parameters \(K\) and \(L\) which describe how the firing rate is transformed into molecular events that are changing the duration and the probability of vesicular release respectively. The time scales \(t_f\) and \(t_r\) define the recovery of a synapse from the network activity. Finally, \(\dot{\omega}\) is an additive Gaussian white noise and \(\sigma\) its amplitude, that represent fluctuations in the firing rate.

The model \([1]\) does not account for long AHP periods, that could be due to potassium channels \([31]\), leading to a refractory period. To account for AHP, we modified the classical depression-facilitation model by introducing two features: 1) A new equilibrium state representing hyperpolarization 2) two timescales, for the medium and slow recovery to steady state.

To implement these novel properties, we decomposed the burst in four steps: step 1 starts with burst initiation and ends when the depression \(y\) starts increasing again, where we consider that hyperpolarization is initiated. Step 2 lasts until \(y\) grows above the threshold \(Y_h\) again. During this phase, we change the time constant \(\tau\) of \(h\) to \(\tau_{mAHP}\) and the resting value of \(h\) from \(T_0\) to \(T_{AHP}\) so that system \([1]\) becomes:

\[
\begin{align*}
\tau_0 \dot{h} &= -(h - T_0) + Jx y (h - T_0)^+ + \sqrt{\tau_0} \sigma \dot{\omega} \\
\dot{x} &= \frac{X - x}{\tau_f} + K(1 - x)(h - T_0)^+ \\
\dot{y} &= \frac{1 - y}{\tau_r} - Lx y (h - T_0)^+ ,
\end{align*}
\]  

(2)

where \(\tau_0 = \tau_{mAHP}\) and \(T_0 = T_{AHP}\) for \(y < Y_h\) and \(\dot{y} > 0\). These changes forces the voltage to hyperpolarize. In step 3 the depression \(y\) is still increasing, that is: \(\dot{y} > 0\), \(Y_{AHP} < y\) and \(h > H_{AHP}\). During this phase, we change the time constant \(\tau_{mAHP}\) to \(\tau_0 = \tau_{sAHP}\) and the resting value of \(h\) is set to its initial value \(T_0 = T\). These modifications accounts for the slow recovery from hyperpolarization to the resting state, this phase end when \(y\) reaches a second threshold \(Y_{AHP}\) and \(h\) reaches another threshold \(H_{AHP}\). Step 4 models the resting state, where \(y > Y_{AHP}\) and \(h \geq H_{AHP}, \tau_0 = \tau\) and \(T_0 = T\). All parameters are defined in Table \([1]\).

We use \([26,28,30]\) to determine the values of the parameters for the classical facilitation-depression part and the order of magnitudes reviewed in \([31]\) for the new AHP parameters \((T_{AHP}, \tau_{mAHP}\) and \(\tau_{sAHP}\), Table \([1]\). We will determine in sections \([2.5.1\) and \([2.6\) the effect on bursting dynamics of varying these parameters.

Numerical simulations of equations \([2]\) with a sufficient level of noise exhibit spontaneous bursts in the voltage variable followed by AHP periods (fig. \([A-B, \text{upper}]\). We segmented the simulated time series into two phases: burst (fig. \([C, \text{blue}]\) and interburst, which is further segmented into a AHP (pink) and quiescent phase (QP, green). We recall that we define the quiescent phase as the period where the voltage fluctuates around its equilibrium \(h = 0\). This segmentation allows us to obtain the distributions of burst, AHP and QP durations (fig. \([D]\).
| Parameters         | Values       |
|--------------------|--------------|
| $\tau$            | Fast time constant for $h$ 0.05s |
| $\tau_{mAHP}$     | Medium time constants for $h$ 0.15s |
| $\tau_{sAHP}$     | Slow time constants for $h$ 5s |
| $J$               | Synaptic connectivity 4.21 |
| $K$               | Facilitation rate 0.037Hz |
| $X$               | Facilitation resting value 0.08825 |
| $L$               | Depression rate 0.028Hz |
| $\tau_f$         | Facilitation time rate 2.9s |
| $\tau_d$         | Depression time rate 0.9s |
| $T$               | Depolarization parameter 0 |
| $\sigma$         | Noise amplitude 3 |
| $T_{AHP}$         | Undershoot threshold -30 |

Table 1: Model parameters

1.2 Phase-space analysis

We describe here the phase-space of the deterministic part of system \([2]\).

1.2.1 Equilibrium points

**Attractor.** The first equilibrium point $A$ is given by $h = 0, x = X, y = 1$ and the Jacobian at this point is

$$J_A = \begin{pmatrix} -1 + JX \tau & 0 & 0 \\ K(1 - X) & -1 \tau_f & 0 \\ LX & 0 & -1 \tau_r \end{pmatrix}. \tag{3}$$

The eigenvalues $\lambda_1 = \frac{-1 + JX}{\tau}, \lambda_2 = \frac{-1}{\tau_f}$ and $\lambda_3 = \frac{-1}{\tau_r}$ are real strictly negative, confirming the nature of the attractor (fig. 1B and 2A, yellow star). Note that with the parameters of Table 1, the system shows three orders of magnitude as $\lambda_1 = -12.6, \lambda_2 = -1.1, \lambda_3 = -0.34$. This shows that the dynamics near the attractor is very anisotrope, very restricted to the plan perpendicular to the eigenvector associated to the highest eigenvalue $|\lambda_1|$.

**Saddle-points.** Another solution of $\dot{h} = 0$ is given by $Jxy = 1$. Then $\dot{x} = 0$ yields

$$\frac{X - x}{\tau_f} + K(1 - x)(h - T - T_0) = 0 \Leftrightarrow h = T + T_0 + \frac{x - X}{\tau_f K(1 - x)},$$

re-injecting $h$ in $\dot{y} = 0$ gives

$$\frac{1 - \frac{1}{Jx}}{\tau_r} - \frac{L X - x}{J \tau_f K(1 - x)} = 0 \Leftrightarrow (J \tau_f K + L \tau_r)x^2 - (\tau_f K(J + 1) + LX \tau_r)x + \tau_f K = 0,$$

the discriminant of this equation is

$$\Delta = (\tau_f K(J + 1) + LX \tau_r)^2 - 4(J \tau_f K + L \tau_r)\tau_f K > 0. \tag{4}$$
Figure 1: **Exploration of the AHP-model.** A. Time series for the mean voltage $h$ (upper, normalized), the facilitation $x$ (center) and the depression $y$ (lower) simulated from eq. (2). B. Three dimensional phase-space of the AHP-model showing a burst trajectory. The trajectory is decomposed into a QP (green), a burst (blue) and an AHP (pink) phase. The phase-space is divided into 3 regions according to the AHP dynamics: 1) the medium dynamics of hyperpolarization $\tau_0 = \tau_{mAHP}$ & $T_0 = T_{AHP}$ under and right of the orange surface where the trajectory is highlighted (orange circles). 2) The slow recovery dynamics ($\tau_0 = \tau_{sAHP}$ & $T_0 = 0$, region under the purple plan) where the trajectory is highlighted (purple triangles). 3) The fast dynamics ($\tau_0 = \tau$ & $T_0 = 0$). C. Segmentation of the voltage time series in burst (blue) and interburst (AHP (pink) and QP (green)). D. Distribution of burst (left, blue), AHP (center, pink) and QP (right, green) durations, extracted from numerical simulations lasting $10^4$s.
Thus

\[
x_{1,2} = \frac{\tau J K (J + 1) + L X \tau_r \pm \sqrt{\Delta}}{2(J \tau J K + L \tau)}
\]

\[
y_{1,2} = \frac{1}{J x_{1,2}}
\]

\[
h_{1,2} = T + T_0 + \frac{x_{1,2} - X}{\tau K (1 - x_{1,2})}.
\]

The Jacobians of the system at these points are

\[
J_{S_{1,2}} = \begin{pmatrix}
0 & J y_{1,2} (h_{1,2} - T - T_0)^+ & J x_{1,2} (h_{1,2} - T - T_0)^+ \\
K (1 - x_{1,2}) & -\frac{1}{\tau_r} - K (h_{1,2} - T - T_0)^+ & 0 \\
-\frac{L}{J} & -L y_{1,2} (h_{1,2} - T - T_0)^+ & -\frac{1}{\tau_r} - L x_{1,2} (h_{1,2} - T - T_0)^+
\end{pmatrix}
\]

With the parameter values of Table 1, \( y_{1,2} > Y_h \) and thus \( T_0 = 0 \). Moreover, \( \dot{y}_{|y_{1,2}} < 0 \) so \( \tau_0 = \tau \).

We compute numerically the eigenvalues of the matrices \( J_{S_{1,2}} \). The first saddle point \( S_1 \) has one real strictly negative eigenvalue and two complex-conjugate eigenvalues with positive real-parts, \( S_1 \) is a saddle-focus (with a repulsive focus and a stable manifold of dimension 1, fig. 2B). The second saddle point \( S_2 \) has two real negative eigenvalues and one positive one, it is a saddle-point with a stable manifold of dimension two and unstable of dimension one (fig. 2C).

1.2.2 Boundary of the basin of attraction associated to the stable equilibrium \( A \)

To determine the boundary of the basin of attraction for the point \( A \), we ran numerical simulations of the deterministic system (no noise), where we sample the entire \((h, x, y)\)-space for the initial points and monitored where the trajectories escaped from the basin of attraction, characterized by a long trajectory, which describes the bursting phase. The limit values for the initial points, where trajectories escape define the separatrix surface \( \Sigma \) (fig. 2, cyan surface). Note that this separatrix \( \Sigma \) is constructed with a precision \( \Delta h = 0.01 \) for a normalized amplitude of \( h \) to 1, which is smaller than the spatial scale of the stochastic component of the simulation \( \sigma \sqrt{\tau \Delta t} \approx 0.07 \).

To characterize the range of bursting durations, we determined numerically the durations of the shortest (red) and longest (purple) trajectories starting in the upper neighborhood of the separatrix \( \Sigma \) and ending below \( h = 0 \) (fig. 2D). The extreme trajectories are determined when we sampled the initial condition in the discretized approximation of \( \Sigma \) by a grid \((x_k, y_q) = (k \Delta x, q \Delta y) \in [0, 1]^2 \), where we use for numerical computation \( \Delta x = \Delta y = 0.025 \).

To better understand how the stochastic system bursts, we studied the distribution of exit points around the basin of attraction of \( A \). We ran simulations with initial point \( A \) and a fixed level of noise, for each burst, and we recorded the intersection point of the trajectory and the separatrix (exit point). We show this distribution of points on the separatrix in fig. 3. In section 1.3 we shall explicitly it analytically.

1.3 Distribution of exit points

We determine now the distribution of exit points located on the separatrix \( \Sigma \) when the initial point is at the attractor \( A = (0, X, 1) \). In this region of the phase-space, the dynamics simplifies to the system
Figure 2: **Phase-space of the dynamical system (2).** A. Repulsive trajectories from the saddle point $S_1$ (pink) and $S_2$ (blue) with corresponding eigenvectors (dashed arrows). B. Inset around $S_1$. Real (dashed red arrow) and imaginary (dashed green arrow, see inset) parts of the eigenvectors associated to the complex conjugate repulsive eigenvalues and attractive eigenvector (dashed blue arrow). C. Inset around $S_2$. Attractive eigenvectors (dashed blue and black arrows), and repulsive one (dashed red arrow). D. Longest (purple) and shortest (red) bursting trajectories starting outside the basin of attraction.
Figure 3: **Stochastic dynamics in the phase-space of fig.2**  
**A.** Exit points (yellow dots on $\Sigma$) of the stochastic system (2) from the basin of attraction (5000s numerical simulations, $\sigma = 3$) with longest (purple) and shortest (red) trajectories.  
**B.** Escaping stochastic trajectory (black), Inset around the attractor $A$ (yellow star).  
**C.** Top view of $A$ and center of mass $C_M$ of the exit points (red cross).  
**D.** Inset of $C$. 
without AHP:

\[
\begin{align*}
\tau \dot{h} &= -h + Jxyh^+ + \sqrt{\tau \sigma} \omega \\
\dot{x} &= \frac{X - x}{\tau_f} + K(1 - x)h^+ \\
\dot{y} &= \frac{1 - y}{\tau_r} - Lxyh^+,
\end{align*}
\]

which can be written in the matrix form

\[
\dot{s} = B(s) + \sqrt{\sigma} \dot{W}
\]

where

\[
B(s) = \begin{pmatrix}
b_1(s) = -\frac{h}{\tau} + \frac{Jxyh^+}{\tau} \\
b_2(s) = \frac{X - x}{\tau_f} + K(1 - x)h^+ \\
b_3(s) = \frac{1 - y}{\tau_r} - Lxyh^+
\end{pmatrix}
\]

and \(\sqrt{\sigma} = \text{diag} \left( \sqrt{\frac{\sigma}{\tau}}, 0, 0 \right)\). The probability density function \(q(s)\) of exit points is obtained by conditioning that the trajectories of the process (8) are absorbed on \(\Sigma\). It is solution of the Fokker-Planck renewal equation (FPE) \[36,37\]

\[
-\frac{\partial}{\partial h} \left[ \frac{(Jxy - 1)h}{\tau} q(s) \right] - \frac{\partial}{\partial x} \left[ \left( \frac{X - x}{\tau_f} + K(1 - x)h \right) q(s) \right] - \frac{\partial}{\partial y} \left[ \left( \frac{1 - y}{\tau_r} - Lxyh \right) q(s) \right] + \frac{\sigma}{2\tau \partial h^2} q(s) = \delta(s - s_0)
\]

(10)

\[
q(s \in \Sigma | s_0) = 0.
\]

(11)

We use WKB approximation to search for a solution of equation (10) in the form

\[
q(s | s_0) = Q_\sigma(s)e^{-\psi(s)/\sigma},
\]

(12)

where \(Q_\sigma\) is a regular function with the formal expansion

\[
Q_\sigma(s) = \sum_{i=0}^{\infty} Q_i(s) \sigma^i.
\]

(13)

The function \(\psi\) satisfies the eikonal equation

\[
\frac{(Jxy - 1)h}{\tau} \frac{\partial \psi}{\partial h} + \left( \frac{X - x}{\tau_f} + K(1 - x)h \right) \frac{\partial \psi}{\partial x} + \left( \frac{1 - y}{\tau_r} - Lxyh \right) \frac{\partial \psi}{\partial y} + \frac{1}{2\tau} \left( \frac{\partial \psi}{\partial h} \right)^2 = 0
\]

(14)

We use the method of characteristics to solve the eikonal equation. Setting

\[
p = \nabla \psi = \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix},
\]

(15)
and using the classical notation

\[ F(s, \psi, p) = b_1(s)p_1 + b_2(s)p_2 + b_3(s)p_3 + \frac{1}{2}p_1^2, \tag{16} \]

the characteristics are given by

\[
\frac{dh}{dt} = F_{p_1} = b_1 + \frac{1}{\tau}p_1 \\
\frac{dx}{dt} = F_{p_2} = b_2 \\
\frac{dy}{dt} = F_{p_3} = b_3, \tag{17}
\]

\[
\frac{dp_1}{dt} = -F_h = -\frac{Jxy - 1}{\tau}p_1 - K(1 - x)p_2 + Lxy p_3 \\
\frac{dp_2}{dt} = -F_x = -\frac{Jyh}{\tau}p_1 + \left(\frac{1}{\tau_f} + Kh\right)p_2 + Lyhp_3 \tag{18} \\
\frac{dp_3}{dt} = -F_y = -\frac{Jxh}{\tau}p_1 + \left(\frac{1}{\tau_r} + Lxh\right)p_3
\]

and

\[
\frac{d\psi}{dt} = \frac{1}{2}p_1^2. \tag{19}
\]

We should solve (17)-(19) starting at the attractor \( s_0 = A \), however, this characteristic will be trapped at \( A \). To avoid this difficulty, we follow the method proposed in [37] p.165-170, and we start from points located in a neighborhood \( V_A \) of \( A \). In \( V_A \), the solution of the eikonal equation has a quadratic approximation

\[
\psi(s) = \frac{1}{2}s^T R s + o(|s|^2). \tag{20}
\]

To find the matrix \( R \), we use the linearized eikonal equation around the attractor \( A \)

\[
(J_A s)^T \cdot \nabla \psi + \frac{1}{2}p_1^2 = 0, \tag{21}
\]

where \( J_A \) is the Jacobian defined in [3]. This matrix equation does not have a unique solution, but we shall use the one given by

\[
\psi(s) \approx (1 - JX) h^2. \tag{22}
\]

Choosing initial conditions on the contours \( \psi(s) = \delta = 0.05 \), that is

\[
h = \pm \sqrt{\frac{\delta}{1 - JX}} \approx 0.28, \tag{23}
\]

we computed the characteristics numerically (fig. 4A-B). To determine the exit points distribution, we now solve the transport equation (24)

\[
\frac{1 - Jxy}{\tau} \left( \frac{\partial Q_0}{\partial h} + Q_0 \right) + \left( \frac{1}{\tau_f} + Kh \right) Q_0 - \left( \frac{X - x}{\tau_f} + K(1 - x)h \right) \frac{\partial Q_0}{\partial x} + \left( \frac{1}{\tau_r} + Lxh \right) Q_0 \\
- \left( \frac{1 - y}{\tau_r} - Lxyh \right) \frac{\partial Q_0}{\partial y} - \frac{1}{\tau} \frac{\partial Q_0 \partial \psi}{\partial h} - \frac{Q_0 \partial^2 \psi}{2\tau \partial h^2} = 0. \tag{24}
\]
To find $Q_0$, we follow the method from [37] p.172-175. We rewrite equation (24)

$$B \cdot \nabla Q_0 + \frac{1}{\tau} \frac{\partial Q_0}{\partial h} \frac{\partial \psi}{\partial h} = - \left( \nabla \cdot B + \frac{1}{2\tau} \frac{\partial^2 \psi}{\partial h^2} \right) Q_0$$

(25)

where $B$ is defined in (9). Along the characteristics, (25) is

$$\frac{dQ_0(s(t))}{dt} = \nabla Q_0(s(t)) \cdot \frac{ds(t)}{dt} = - \left( \nabla \cdot B(s(t)) + \frac{1}{2\tau} \frac{\partial^2 \psi(s(t))}{\partial h^2} \right) Q_0(s(t))$$

(26)

Our goal is to compute $Q_0$ on the separatrix and for that purpose, we need to evaluate $\frac{\partial^2 \psi(s(t))}{\partial h^2}$ by differentiating the characteristics equations (17)-(19) with respect to the initial point $s_0 = s(0)$. Setting

$$s_j(t) = \frac{\partial s(t)}{\partial s_0^j}, \quad p_j(t) = \frac{\partial p(t)}{\partial s_0^j}, \quad \frac{\partial^2 \psi(s(t))}{\partial s^i \partial s^j} = R^{i,j}(t),$$

(27)

we have $R(t) = P(t)S(t)^{-1}$, where $P(t)$ (resp. $S(t)$) is the matrix with columns $p_j(t)$ (resp. $s_j(t)$). The initial conditions are

$$s_j^i(0) = \delta_{i,j}, \quad p_j^i(0) = \frac{\partial^2 \psi(0)}{\partial s^i \partial s^j} = R^{i,j}.$$  

(28)

The dynamic has the form

$$\frac{ds_1^1(t)}{dt} = \frac{dh_1}{dt} = \frac{\partial b_1}{\partial h} + \frac{1}{\tau} \frac{\partial p_1}{\partial h} h_1$$

$$\frac{ds_2^2(t)}{dt} = \frac{dh_2}{dt} = \frac{\partial b_2}{\partial h} + \frac{1}{\tau} \frac{\partial p_2}{\partial h} h_2$$

$$\frac{ds_3^3(t)}{dt} = \frac{dh_3}{dt} = \frac{\partial b_3}{\partial h} + \frac{1}{\tau} \frac{\partial p_3}{\partial h} h_3$$

$$\frac{dx_1}{dt} = \frac{\partial b_2}{\partial x} x_1$$

$$\frac{dx_2}{dt} = \frac{\partial b_2}{\partial x} x_2$$

$$\frac{dx_3}{dt} = \frac{\partial b_2}{\partial x} x_3$$

$$\frac{dy_1}{dt} = \frac{\partial b_3}{\partial y} y_1$$

$$\frac{dy_2}{dt} = \frac{\partial b_3}{\partial y} y_2$$

$$\frac{dy_3}{dt} = \frac{\partial b_3}{\partial y} y_3$$

(29)
and because we are only interested in $R^{1,1}$ we only need to compute the first row of $P(t)$, thus

$$
\frac{dp_1^1(t)}{dt} = \left( -\frac{Jxy - 1}{\tau} \frac{\partial p^1}{\partial h} - K(1 - x) \frac{\partial p^2}{\partial h} + Lxy \frac{\partial p^3}{\partial h} \right) h_1
$$

$$
\frac{dp_2^1(t)}{dt} = \left( -\frac{Jxy - 1}{\tau} \frac{\partial p^1}{\partial h} - K(1 - x) \frac{\partial p^2}{\partial h} + Lxy \frac{\partial p^3}{\partial h} \right) h_2
$$

$$
\frac{dp_3^1(t)}{dt} = \left( -\frac{Jxy - 1}{\tau} \frac{\partial p^1}{\partial h} - K(1 - x) \frac{\partial p^2}{\partial h} + Lxy \frac{\partial p^3}{\partial h} \right) h_3.
$$

(30)

In the limit $t \to \infty$ the characteristic that hits the saddle point $S_2$ is tangent to the separatrix and $-\left( \nabla \cdot B + \frac{1}{2\tau} \frac{\partial^2 \psi}{\partial h^2} \right) Q_0 \to -\nabla \cdot B|_{S_2} \approx 1.82$. Indeed, $\frac{\partial^2 \psi}{\partial h^2}$ tends to 0 near the saddle point $S_2$ as shown in fig. 4C. Thus, near the saddle point, we have

$$
\frac{dQ_0(s(t))}{dt} = -(\nabla \cdot B_{|S_2} + o(1)) Q_0(s(t)).
$$

(31)

The solution is approximated by

$$
Q_0(s(t)) = Q_0(s(0)) e^{-\nabla \cdot B_{|S_2} t(1 + o(1))}.
$$

(32)

Finally, the characteristic $s(t)$ near the saddle point $S_2$ can be expressed with respect to the arc length $\tilde{s}$:

$$
\tilde{s}(t) \approx \int_0^t \sqrt{s_2(u)^2} du,
$$

(33)

where $s_2$ is the dominant coordinate of $s \in \Sigma$ in the eigenvectors basis of the jacobian $J_{S_2}$ of system (2) at $S_2$, ($\lambda_1 \approx -4.58$ and $\lambda_2 \approx -0.25$), thus locally

$$
\tilde{s}(t) \approx \int_0^t \sqrt{s_2(0)^2} e^{2\lambda_2 u} du,
$$

(34)

and

$$
\tilde{s}(t) \approx \int_0^t \sqrt{s_2(0)^2} e^{2\lambda_2 u} du = s_2(0) e^{\lambda_2 t} - \frac{1}{\lambda_2}.
$$

(35)

Finally, using (32) and (35), we obtain locally

$$
Q_0(\tilde{s}) = Q_0(0) \tilde{s} \frac{\nabla \cdot B_{|S_2}}{\lambda_2},
$$

(36)

where $-\nabla \cdot B_{|S_2} \approx -7.23$.

To connect the solution $q$ of the FPE (10) to the distribution of exit points, we have to account for the boundary layer function $q_\sigma$ that has to be added to the transport solution in the form $Q_0 q_\sigma$. This product satisfies the boundary condition (11). We do not compute here $q_\sigma$ as the computation follows the one of [37] p. 182-183 near the separatrix. It is a regular function of the form $-\sqrt{\frac{2}{\pi}} \int_0^{\rho \gamma(s_1,s_2)/\sqrt{\sigma}} e^{-\eta^2/2} d\eta$, where $\rho$ is the distance to the separatrix $\Sigma$ in a neighborhood of $S_2$ and $\gamma(s_1,s_2)$ a regular function.
Finally, we recall that the exit point distribution per unit surface $d\mathbf{s}$ is given by

$$p_{\Sigma}(\tilde{s}|\mathbf{s}_0) = \frac{1}{N} J(\tilde{s}|\mathbf{s}_0) \cdot \nu(\tilde{s}) d\tilde{s} \text{ for } \tilde{s} \in \Sigma$$

(37)

where the probability flux is

$$J(\tilde{s}|\mathbf{s}_0) = \begin{pmatrix} J_{xy} - \frac{1}{\tau} h q(\tilde{s}) - \sigma \frac{\partial q(\tilde{s})}{\partial \mathbf{h}} \\ \frac{X - x}{\tau_x} + K(1 - x) h q(\tilde{s}) \\ \left( \frac{1 - y}{\tau_y} - L_{xy} h \right) q(\tilde{s}) \end{pmatrix},$$

(38)

and the normalization constant is

$$N = \oint_{\Sigma} J(\tilde{s}|\mathbf{s}_0) \cdot \nu(\tilde{s}) d\tilde{s},$$

(39)

where $\nu(\tilde{s})$ is the unit normal vector at the point $\tilde{s}$. The flux is computed by differentiating expression (12),

$$q(\tilde{s}|\mathbf{s}_0) = q_\sigma(\tilde{s}) Q_0(\tilde{s}) e^{-\frac{\psi(\tilde{s})}{\sigma}}.$$  

(40)

We obtain

$$J(\tilde{s}|\mathbf{s}_0) \cdot \nu(\tilde{s}) d\tilde{s} = -N \sqrt{\frac{2\sigma}{\pi}} q(\tilde{s}|\mathbf{s}_0) \gamma(s_1, s_2) d\tilde{s}$$

$$= K_0 \tilde{s} \frac{\nabla \cdot B_{|s_2}}{\lambda_2} e^{-\frac{\psi(\tilde{s})}{\sigma}} d\tilde{s},$$

(41)

where $\gamma(s_1, s_2)$ has been approximated by its value at $\tilde{s} = 0$. Furthermore, in the limit $\tilde{s} \to 0$, $\tilde{s} \frac{\nabla \cdot B_{|s_2}}{\lambda_2}$ tends to infinity, however it is compensated by $e^{-\frac{\psi(\tilde{s})}{\sigma}}$ which is small enough, as we observe numerically.

We plotted the distribution of exit points in fig. 4D-E for $K_0 = 1$. Finally, we compare the distribution $p_{\Sigma}$ with the one obtained from the stochastic simulations of system (2) with the same level of noise ($\sigma = 3$). Both distributions are peaked, showing that the exit points are constrained in a small area of the separatrix.

To conclude this part, our two different numerical methods confirm that the exit point distribution is peaked, thus the trajectories associated to the bursting periods are confined in a tubular neighborhood of a generic trajectory and thus the distribution of the bursting times is peaked, as observed in fig. 1D.
Figure 4: Exit probability. A-B. Characteristics crossing the separatrix $\Sigma$ (the darker the line color is, the lower the value of $\psi$ on $\Sigma$ is) and distribution exit points obtained from numerical simulations (yellow); visualized with two different angles. C. $R^{1,1}(t) = \frac{\partial^2 \psi}{\partial h^2}$ vs time along the characteristic, obtained numerically. D-E. PDF of the exit points $p_\Sigma = Q_0e^{-\frac{\psi}{\sigma}}$ on the separatrix $\Sigma$ compared to the distribution obtained from the stochastic simulations (white histogram); visualized with two different angles.
2 Computing analytically burst and AHP durations

2.1 Approximated equations

In this section we develop an approximation procedure to compute the mean bursting and hyperpolarization durations from the AHP facilitation-depression model (2).

The approximation procedure is based on the following considerations: because in the first phases of burst and AHP, the voltage $h$ evolves much faster than the facilitation $x$ and depression $y$, to compute the duration of the bursting phase, we will replace the dynamics of $h$ in the depression and facilitation equations by a piecewise constant function $H(t)$ (fig.5). This approximation decouples the system (2), thus $x$ and $y$ can be computed.

We shall now specify the function $H(t)$. In the bursting phase, it is constant equal to $H_1$ for $t \in [0; t_1]$ where $t_1$ will be specified in section 2.4. In the hyperpolarization phase, $H(t) = H_2$ for $t \in [0; t_2]$. For $t > t_2$ (that will also be specified in section 2.4), we choose $H(t) = 0$ to account for the recovery phase.

\[
H(t) = \begin{cases} 
H_1, & \text{for } t \in [0, t_1] \\
H_2, & \text{for } t \in [t_1, t_2] \\
0, & \text{for } t > t_2.
\end{cases}
\] (42)

The approximated system of equations becomes:

\[
\begin{align*}
\tau_0 \frac{dh}{dt} &= -(h - T_0(t)) + Jxy(h - T_0(t)) + Jxy(h - T_0(t))H(t) \\
\dot{x} &= \frac{X - x}{\tau_f} + K(1 - x)H(t) \\
\dot{y} &= \frac{1 - y}{\tau_r} - LxyH(t)
\end{align*}
\] (43)

where the AHP is accounted for by changing the threshold and timescales as follows

\[
T_0(t) = \begin{cases} 
0, & \text{for } t \in [0, t_1] \\
T_{AHP}, & \text{for } t \in [t_1, t_2] \\
0, & \text{for } t > t_2
\end{cases}
\]

and

\[
\tau_0(t) = \begin{cases} 
\tau, & \text{for } t \in [0, t_1] \\
\tau_{mAHP}, & \text{for } t \in [t_1, t_2] \\
\tau_{sAHP}, & \text{for } t > t_2.
\end{cases}
\] (44)

2.2 Computing the facilitation and depression dynamics in three phases

Phase 1

We integrate the facilitation and depression equations in (43). During the bursting phase (fig. 5, phase 1, blue) $H(t) = H_1$. We use the following initial conditions: $x(0) = X$ and $y(0) = 1$ (resting values). We obtain

\[
x(t) = A_1 e^{-\alpha_1 t} + B_1,
\] (45)

where

\[
\begin{align*}
\alpha_1 &= \frac{1}{\tau_f} + KH_1, \\
A_1 &= \frac{KH_1(X - 1)}{\alpha_1}, \\
B_1 &= \frac{X}{\tau_f} + KH_1
\end{align*}
\] (46)

Injecting expression (45) in the third equation of system (43), we obtain

\[
\dot{y} = \frac{1 - y}{\tau_r} - L(A_1 e^{-\alpha_1 t} + B_1)H_1 y
\]
Phase 1

1. Burst: fast timescale $\tau_0 = \tau$, no hyperpolarization: $T_0 = 0$

2. AHP initiation: medium timescale $\tau_0 = \tau_{mAHP}$, hyperpolarization: $T_0 = T_{AHP} < 0$

3. Recovery: slow timescale $\tau_0 = \tau_{sAHP}$, no hyperpolarization: $T_0 = 0$

Figure 5: Approximated voltage step function $H(t)$.

The solution is

$$y(t) = \left( C_1 + \frac{1}{\tau_r} \int_0^t \exp(f_1(s))ds \right) \exp(-f_1(t)), \quad (47)$$

where the function

$$f_1(t) = \beta_1 t - \frac{LA_1 H_1}{\alpha_1} e^{-\alpha_1 t}. \quad (48)$$

To approximate the integral $\int_0^t \exp(f_1(s))ds$, we use that $f_1$ is monotonic on the interval $[0; t_1]$, thus using a Taylor expansion at order 1, we get

$$\int_0^t \exp(f_1(s))ds \approx \exp(f_1(t)) \int_0^t \exp(f_1'(t)(s-t))ds = \frac{\exp(f_1(t))}{f_1'(t)} (1 - \exp(-tf_1'(t))). \quad (49)$$

Using expression (47), we obtain the approximation for $t \in [0, t_1]$

$$y(t) \approx \left( \frac{1}{\tau_r} \frac{(1 - \exp(-tf_1'(t)))}{f_1'(t)} \right) + C_1 \exp(-f_1(t)), \quad (49)$$

where

$$\beta_1 = \frac{1}{\tau_f} + B_1 LH_1 \quad \text{and} \quad C_1 = \exp \left( -\frac{LH_1 A_1}{\alpha_1} \right). \quad (50)$$

Phase 2

The second phase starts at $t_1$ where $H(t) = H_2$, where the equations and the approximation are similar to the paragraph above. However we use the following initial conditions: $x(t^-_1) = x(t^+_1)$ and $y(t^-_1) = y(t^+_1)$. This yields for $t \in [t_1; t_2]$,

$$x(t) = A_2 e^{-\alpha_2 t} + B_2, \quad (51)$$

where

$$\alpha_2 = \frac{1}{\tau_f} + KH_2, \quad A_2 = (x(t^-_1) - B_2)e^{\alpha_2 t_1}, \quad B_2 = \frac{X}{\tau_f} + KH_2. \quad (52)$$
\[ y(t) \approx \left( \frac{1}{\tau_r} \left( 1 - \exp\left(-\left(t - t_1\right)f_2(t)\right) \right) \right) + C_2 \exp(-f_2(t)), \]

where
\[ f_2(t) = \beta_2 t - \frac{LA_2 H_2}{\alpha_2} e^{-\alpha_2 t}, \tag{53} \]
\[ \beta_2 = \frac{1}{\tau_r} + B_2 LH_2 \text{ and } C_2 = y(t_1^-) \exp(f_2(t_1^-)). \tag{54} \]

**Phase 3**

The recovery phase starts at \( t_2 \) where \( H(t) = 0 \). We use the following initial conditions: \( x(t_2^-) = x(t_2^+) \) and \( y(t_2^-) = y(t_2^+) \). This yields for \( t \geq t_2 \) to the solution
\[ x(t) = X + (x(t_2^-) - X) \exp\left(-\frac{t - t_2}{\tau_f}\right) \tag{55} \]
\[ y(t) = 1 + (y(t_2^-) - 1) \exp\left(-\frac{t - t_2}{\tau_r}\right). \]

**2.3 Computing the approximated voltage in the three phases**

To compute the voltage, we will use the approximations for \( x \) and \( y \) described for the three phases in paragraph 2.2. Although the previous approximations might be drastic for \( x \) and \( y \), we shall see that they provide a very good approximation for \( h \). In addition, they allowed to decouple the system of equations and thus \( h \) can now be computed explicitly.

**Phase 1**

The first equation in system (43) is
\[ \tau \dot{h} = -h + Jxyh^+ \tag{56} \]
where the initial condition is \( h(0) = \bar{H}_1 \). A direct integration leads to
\[ h(t) = \bar{H}_1 \exp\left(-\frac{t}{\tau} + \frac{J}{\tau} \int_0^t x(s)y(s)ds\right). \tag{57} \]

To obtain an explicit dependency of the solution \( h \) with respect to the parameters, we will use expressions (45) and (49) for \( x \) and \( y \) respectively to compute the integral in expression (57). This calculation is detailed in appendix A. We note that \( \bar{H}_1 \) could be different from \( H_1 \), indeed to guarantee that the facilitation and depression, that have slower dynamics compared to the voltage, are immediately in the bursting state we choose \( H_1 \gg \bar{H}_1 \) (see Table 3).

**Phase 2**

In phase 2, we use equation (44) for \( T_0 = T_{AHP} \) and \( \tau_0 = \tau_{mAHP} \) so that
\[ \tau_{mAHP} \dot{h} = -(h - T_{AHP}) + Jxy(h - T_{AHP})^+. \tag{58} \]

We use the initial condition \( h(t_1^+) = h(t_1^-) \), and obtain by a direct integration
\[ h(t) = (h(t_1^-) - T_{AHP}) \exp\left(-\frac{t - t_1}{\tau_{mAHP}} + \frac{J}{\tau_{mAHP}} \int_{t_1}^t x(s)y(s)ds\right) + T_{AHP}. \tag{59} \]

Similar to phase 1, we detail this calculation in appendix A.
Phase 3

Finally, when \( t > t_2 \), \( h \) enters into its slow relaxation phase leading in equation (44) to \( T_0 = 0 \) and \( \tau_0 = \tau_{sAHP} \), and the initial condition \( h(t_2^-) = h(t_2^+) \). A direct integration of equation (43) leads to

\[
h(t) = h(t_2^-) \exp \left( -\frac{t - t_2}{\tau_{sAHP}} + \frac{J}{\tau_{sAHP}} \int_{t_2}^{t} x(s)y(s)ds \right).
\]

(60)

Figure 6: Analytical approximation (green) vs exact solution (dashed magenta) for \( h \), \( x \) and \( y \).

2.4 Identification of the termination times \( t_1 \) and \( t_2 \)

End of phase 1

Following burst activation, medium and slow \( K^+ \) channels start to be activated forcing the voltage to hyperpolarize. To account for the overall changes in the voltage dynamics due to this \( K^+ \) channels activation, we change the recovery timescale \( \tau_0 \) to \( \tau_{mAHP} \) (equation (44)) and \( H(t) \) to \( H_2 \) in (42) at time \( t_1 \). In practice the hyperpolarization initiation is defined in the region where \( h \) is decreasing after
reaching its maximum, as the first time $t_1$ where $h(t_1) = h_0$ (expression (57)), leading to equation

$$t_1 \frac{B_1 J - \tau_r \beta_1}{\beta_1 J} = -\frac{1}{\tau_r L \alpha_1 \beta_1} \ln \left( 1 + \frac{L A_1 H_1 e^{-\alpha_1 t_1}}{\beta_1} \right) + \frac{e^{-\alpha_1 t_1} - 1}{\alpha_1} \frac{L A_1 H_1 B_1}{\beta_1} + \frac{e^{-2\alpha_1 t_1} - 1}{2\alpha_1} \frac{(L A_1 H_1)^2 B_1}{\beta_1}$$

$$+ \frac{e^{-(\beta_1 + L A_1 H_1) t_1} - 1}{\beta_1 + L A_1 H_1} \frac{B_1 (1 - \tau_r \beta_1)}{\beta_1} + \frac{e^{-\alpha_1 \beta_1 + L A_1 H_1 t_1} - 1}{\alpha_1 + \beta_1 + L A_1 H_1} A_1 (-\tau_r \beta_1^2 + \beta_1 - L H_1 B_1)$$

$$+ \frac{e^{-(2\alpha_1 + \beta_1 + L A_1 H_1) t_1} - 1}{2\alpha_1 + \beta_1 + L A_1 H_1} \left( \frac{L A_1^2 H_1}{\tau_r \beta_1^2} + \frac{(L A_1 H_1)^2 B_1}{\tau_r \beta_1^2} \right) + \frac{e^{-(3\alpha_1 + \beta_1 + L A_1 H_1) t_1} - 1}{3\alpha_1 + \beta_1 + L A_1 H_1} \frac{L^2 A_1^3 H_1^2}{\tau_r \beta_1^3}$$

$$= \frac{1}{\Gamma_1} \left( -\Gamma_2 \ln \left( \frac{1}{1 + \Gamma_3} \right) + \frac{\Gamma_4}{\alpha_1} + \frac{\Gamma_5}{\beta_1 + L A_1 H_1} + \frac{\Gamma_6}{\alpha_1 + \beta_1 + L A_1 H_1} + \frac{\Gamma_7}{2\alpha_1 + \beta_1 + L A_1 H_1} \right)$$

$$+ \frac{\Gamma_8}{3\alpha_1 + \beta_1 + L A_1 H_1} + \frac{\Gamma_9}{2\alpha_1} + \frac{\tau}{J} \ln \left( \frac{h_0}{H_1} \right) + \frac{\tau}{J} \ln \left( \frac{h_0}{H_1} \right),$$

(61)

This transcendental equation cannot be solved explicitly however, with the parameters from Table 1 and Table 3 and the order of $t_1$, we can neglect the exponential terms in (61), leading to

$$t_1 = \frac{1}{\Gamma_1} \left( -\Gamma_2 \ln \left( \frac{1}{1 + \Gamma_3} \right) + \frac{\Gamma_4}{\alpha_1} + \frac{\Gamma_5}{\beta_1 + L A_1 H_1} + \frac{\Gamma_6}{\alpha_1 + \beta_1 + L A_1 H_1} + \frac{\Gamma_7}{2\alpha_1 + \beta_1 + L A_1 H_1} \right)$$

$$+ \frac{\Gamma_8}{3\alpha_1 + \beta_1 + L A_1 H_1} + \frac{\Gamma_9}{2\alpha_1} + \frac{\tau}{J} \ln \left( \frac{h_0}{H_1} \right),$$

(62)

where

$$\Gamma_1 = \frac{B_1 J - \tau_r \beta_1}{\tau_r \beta_1 J}, \quad \Gamma_2 = -\frac{1}{\tau_r L \alpha_1 \beta_1}, \quad \Gamma_3 = \frac{L A_1 H_1}{\beta_1}, \quad \Gamma_4 = \frac{L A_1 H_1 B_1}{\tau_r \beta_1^2}, \quad \Gamma_5 = \frac{B_1 (1 - \tau_r \beta_1 e^{L A_1 H_1})}{\tau_r \beta_1},$$

$$\Gamma_6 = \frac{A_1 (-\tau_r \beta_1^2 e^{L A_1 H_1}) + \beta_1 - L H_1 B_1}{\tau_r \beta_1^3}, \quad \Gamma_7 = \frac{L A_1^2 H_1}{\tau_r \beta_1^2} \left( \frac{L H_1 B_1}{\beta_1} - 1 \right), \quad \Gamma_8 = \frac{L^2 A_1^3 H_1^2}{\tau_r \beta_1^3} \quad \text{and} \quad \Gamma_9 = -\frac{(L A_1 H_1)^2 B_1}{\tau_r \beta_1^3}. $$

(63)

Using the parameter values from Table 1 and Table 3 we obtain $t_1 \approx 200$ ms. This time suggests that the medium and slow $K^+$ channels start to be activated quite early following burst initiation.

**End of phase 2**

The second phase, dominated by the hyperpolarization, ends when the voltage reaches asymptotically its minimum. In practice we introduce a threshold $h_{AHP}$ so that when $h(t_2) = h_{AHP}$ (expression (59)),
we switch into the third phase (see (42) and (44)). This leads to equation

\[
(t_2 - t_1) \frac{B_2 J - \tau_r \beta_2}{\tau_r \beta_2 J} = \frac{1}{\tau_r H_2 \alpha_2} \ln \left( \frac{1 + \frac{L A_2 H_2 e^{-\alpha_2 t_1} e^{-\alpha_2 (t_2 - t_1)}}{\beta_2}}{1 + \frac{L A_2 H_2 e^{-\alpha_2 t_1}}{\beta_2}} \right) + \frac{e^{-\alpha_2 (t_2 - t_1)} - 1}{\alpha_2} \frac{L A_2 H_2 B_2}{\tau_r \beta_2^2}
\]

\[
- \frac{e^{-2\alpha_2 (t_2 - t_1)} - 1}{2\alpha_2} e^{-2\alpha_2 t_1} \frac{(L A_2 H_2)^2 B_2}{\tau_r \beta_2^3} + \frac{e^{-(\beta_2 + L A_2 H_2) (t_2 - t_1)} - 1}{\beta_2 + L A_2 H_2} e^{-(\beta_2 + L A_2 H_2) t_1} B_2 (1 - C_2 e^{L A_2 H_2^2 e^{-\beta_2} \tau_r \beta_2})
\]

\[
+ \frac{e^{-2\alpha_2 (t_2 - t_1)} - 1}{2\alpha_2} e^{-2\alpha_2 t_1} \frac{(L A_2 H_2)^2 B_2}{\tau_r \beta_2^3} = \frac{\tau_{mAHP}}{J} \ln \left( \frac{h_{AHP} - T_{AHP}}{h(t_1) - T_{AHP}} \right).
\]

Here all terms are of the same order thus we cannot neglect any of them. Since we just need to estimate the value of \( t_2 \) to calibrate our approximated model we solve numerically the following transcendental equation

\[
\Lambda_1 (t_2 - t_1) + \Lambda_2 \ln \left( \frac{1 + \Lambda_3 e^{-\alpha_2 (t_2 - t_1)}}{1 + \Lambda_3} \right) + \Lambda_4 \frac{e^{-\alpha_2 (t_2 - t_1)} - 1}{\alpha_2} + \Lambda_5 \frac{e^{-(\beta_2 + L A_2 H_2) (t_2 - t_1)} - 1}{\beta_2 + L A_2 H_2}
\]

\[
+ \Lambda_6 \frac{e^{-2\alpha_2 (t_2 - t_1)} - 1}{2\alpha_2} e^{-2\alpha_2 t_1} \frac{(L A_2 H_2)^2 B_2}{\tau_r \beta_2^3} = \frac{\tau_{mAHP}}{J} \ln \left( \frac{h_{AHP} - T_{AHP}}{h(t_1) - T_{AHP}} \right) = 0,
\]

where

\[
\Lambda_1 = \frac{B_2 J - \tau_r \beta_2}{\tau_r \beta_2 J}, \quad \Lambda_2 = -\frac{1}{\tau_r H_2 \alpha_2}, \quad \Lambda_3 = \frac{L A_2 H_2}{\beta_2} e^{-\alpha_2 t_1}, \quad \Lambda_4 = \frac{L A_2 H_2 B_2}{\tau_r \beta_2^2} e^{-\alpha_2 t_1},
\]

\[
\Lambda_5 = \frac{B_2 (1 - \tau_r \beta_2 C_2 e^{L A_2 H_2^2} e^{-\alpha_2} \tau_r \beta_2)}{\tau_r \beta_2} e^{-(\beta_2 + L A_2 H_2) t_1},
\]

\[
\Lambda_6 = \frac{A_2 (-C_2 e^{L A_2 H_2^2} e^{-\alpha_2} \tau_r \beta_2 + \beta_2 - L H_2 B_2) e^{-(\alpha_2 + \beta_2 + L A_2 H_2) t_1}}{\tau_r \beta_2},
\]

\[
\Lambda_7 = \frac{L A_2 H_2^2}{\tau_r \beta_2^2} \left( \frac{L H_2 B_2}{\beta_2} - 1 \right) e^{-2\alpha_2 + \beta_2 + L A_2 H_2 t_1},
\]

\[
\Lambda_8 = \frac{L A_2 H_2^2}{\tau_r \beta_2^3} e^{-2\alpha_2 + \beta_2 + L A_2 H_2 t_1} \quad \text{and} \quad \Lambda_9 = \frac{(L A_2 H_2)^2 B_2}{\tau_r \beta_2^3} e^{-2\alpha_2 t_1}.
\]

Using parameter values defined in Table 1 and Table 3 and the value of \( t_1 \) computed in the previous section we obtain \( t_2 \approx 1.4 \) s. The obtained analytical approximation is plotted in fig. 6 (green) in comparison to the exact solution obtained using numerical simulations (dashed magenta).
2.5 Bursting and AHP durations

Bursting duration

The burst duration is defined from the voltage jump at time $t = 0$ to $h(t) = H_1$ and ends when $h(t_i) = 0$ for the first time. In practice, we use expression (59) as in section 2.4 for the end of phase 2 however, here $t_i - t_1$ is small enough to allow us to use Taylor expansions to second order leading to the quadratic equation

$$\tilde{\Lambda}(t_i - t_1)^2 + \Lambda(t_i - t_1) - \frac{\tau_m AHP}{J} \ln \left( \frac{-T_{AHP}}{h(t_1^-) - T_{AHP}} \right) = 0,$$

where

$$\tilde{\Lambda} = \left( \frac{\Lambda_2 \Lambda_3 \alpha_2^2}{2(1 + \Lambda_3)^2} + \frac{1}{2} \alpha_2 \Lambda_4 + (\beta_2 + LA_2 H_2) \Lambda_5 + (\alpha_2 + \beta_2 + LA_2 H_2) \Lambda_6 + (2 \alpha_2 + \beta_2 + LA_2 H_2) \Lambda_7 \right. \left. + (3 \alpha_2 + \beta_2 + LA_2 H_2) \Lambda_8 + 2 \alpha_2 \Lambda_9 \right),$$

and

$$\Lambda = \left( -\frac{\Lambda_2 \Lambda_3 \alpha_2}{1 + \Lambda_3} + \Lambda_1 - \Lambda_4 - \Lambda_5 - \Lambda_6 - \Lambda_7 - \Lambda_8 - \Lambda_9 \right).$$

We keep the positive root

$$t_i = t_1 + \sqrt{\frac{\Lambda^2 + 4 \tilde{\Lambda} \tau_m AHP}{J} \ln \left( \frac{-T_{AHP}}{h(t_1^-) - T_{AHP}} \right)} - \Lambda \cdot \frac{\tau_m AHP}{J} \ln \left( \frac{-T_{AHP}}{h(t_1^-) - T_{AHP}} \right).$$

Using parameters from Table 1 and Table 3 we obtain $t_i \approx 940$ ms, which is comparable to the bursting times observed in experimental data[38], and from our numerical simulations (fig. 1D).

AHP duration

The AHP starts at time $t_i$ computed above, however using expression (60) the termination time would be infinite. Thus, we introduce a threshold $\epsilon$ and define the end of AHP $t_e$ such as $h(t_e) = \epsilon$. In practice, the value $\epsilon$ can be estimated from the amplitude of the voltage fluctuations at equilibrium. We obtain from expression (60)

$$-\frac{1}{J} + X \left( t_e - t_2 \right) - \tau_r X (y(t_2^-) - 1) \left( \frac{-t_e - t_2}{e^{\tau_r} - 1} - \tau_f (x(t_2^-) - X) \left( \frac{-t_e - t_2}{e^{\tau_f} - 1} \right) \right. \left. \right.$$ \begin{align*} \left. - \frac{(y(t_2^-) - 1)(x(t_2^-) - X)\tau_f \tau_r}{\tau_f + \tau_r} \right) \right) = \tau_s AHP \frac{J}{J} \ln \left( \frac{\epsilon}{h(t_2^+)} \right), \end{align*}

because $t_e - t_2$ is large enough, we neglect the exponential terms so that

$$(t_e - t_2) \left( X - \frac{1}{J} \right) + \tau_r X (y(t_2^-) - 1) + \tau_f (x(t_2^-) - X) + \frac{(x(t_2^-) - X)(y(t_2^+) - 1)\tau_f \tau_r}{\tau_f + \tau_r} = \tau_s AHP \frac{J}{J} \ln \left( \frac{\epsilon}{h(t_2^+)} \right),$$

$$t_e = t_1 + \sqrt{\frac{\Lambda^2 + 4 \tilde{\Lambda} \tau_m AHP}{J} \ln \left( \frac{-T_{AHP}}{h(t_1^-) - T_{AHP}} \right)} - \Lambda \cdot \frac{\tau_m AHP}{J} \ln \left( \frac{-T_{AHP}}{h(t_1^+) - T_{AHP}} \right).$$
leading to
\[ t_e = t_2 + \left( \frac{\tau_{sAHP}}{J} \ln \left( \frac{\epsilon}{\bar{h}_2} \right) - \tau_r X (y(t_2) - 1) - \tau_f (x(t_2) - X) - \frac{(x(t_2^0) - X)(y(t_2^0) - 1)\tau_f\tau_r}{\tau_f + \tau_r} \right) \frac{J}{JX - 1}. \]

Using the parameter values from Table 1 and Table 3 we obtain \( t_e \approx 15.4 \) s and \( \Delta_{AHP} \approx 14.4 \) s, which is coherent with the durations obtained from the numerical simulations (fig. 1D), as well as classical AHP durations found in the literature [31].

### 2.5.1 Study of parameter influence on burst and AHP durations

To evaluate the influence of the main parameters on the bursting and AHP durations we plotted these times vs the recovery timescales \( \tau_{mAHP} \) and \( \tau_{sAHP} \), the hyperpolarization level \( \bar{T}_{AHP} \) and the arbitrary thresholds \( h_0, \bar{H}_1, h_{AHP} \) and \( \epsilon \). First, the burst duration that varies between 0.5 and 3s, is an increasing function of \( \tau_{mAHP} \) and does not depend much on \( \bar{T}_{AHP} \) in the range \([-15; -40]\) (fig. 7A). In addition, the AHP duration increases with \( \tau_{sAHP} \), but in a larger range from 9 to 35s. However, the hyperpolarization level \( T_{AHP} \) has a larger influence on this duration (fig. 7B). To verify that the arbitrary thresholds that we use do not influence much the burst and AHP durations, we plotted them in fig. 7C-F with respect to the phase 1 termination threshold \( h_0 \), the phase 2 termination threshold \( h_{AHP} \), the duration of phase 1 \( t_1 \) and the AHP termination threshold \( \epsilon \) respectively. These figures show that there is almost no dependency with respect to \( \bar{H}_1 \) and \( T_{AHP} \), as well as \( h_0 \) and \( h_{AHP} \) due to the effect of the logarithmic term.

### 2.6 Numerical analysis of burst and interburst durations: effect of J, K, L parameters

To study the influence of the network connectivity \( J \) on burst, AHP and QP durations, we ran numerical simulations of the stochastic system (2), where we varied \( J \), as well as the facilitation and depression parameters \( K \) and \( L \). To determine the time distributions of burst and interburst, we segmented the traces obtained for 5000 seconds simulations with a noise amplitude \( \sigma = 6 \) and computed the mean value of the bursts (fig. 8A), AHP (fig. 8B) and QP durations (fig. 8C). Interestingly, we observe two different regimes depending on the values of the parameters: no bursts (\( J < 3.05 \) for \( K = 0.047, L = 0.028; J < 3.2 \) for \( K = 0.037, L = 0.028; J < 3.5 \) for \( K = 0.027, L = 0.028 \); fig. 8 left column, or \( J < 3.7 \) for \( K = 0.037, L = 0.038 \) and \( J < 4.1 \) for \( K = 0.037, L = 0.048 \), right column) and bursts followed by AHP (for higher values of \( J \)). Surprisingly, in the bursting regime changing \( J \) does not influence the mean burst duration. However, AHP durations decreases as \( J \) increases. Finally, QP durations reach a peak at the transition value of \( J \) between the two regimes and then quickly decrease around \( QP \approx 25s \). We note that the mean burst durations obtained here are longer than the ones observed in fig. 1D, this is due to the fact that in these simulations, we used \( \sigma = 6 \) (vs \( \sigma = 3 \) for fig. 1D). Indeed, increasing the noise increases the mean burst duration because, at the beginning of the burst, the deterministic part of the trajectory is still perturbed by the noise component, leading to a longer trajectory when the noise level is higher.

To conclude, a sufficient connectivity level is necessary to generate bursting, however once the dynamics enter into this regime, increasing the level of neuronal connectivity does not change much the bursting times.
Figure 7: **Parameter influence on burst and AHP durations.**

A. Evolution of the burst duration $t_i$ as a function of the medium timescale $\tau_{mAHP}$ for multiple values of the hyperpolarization level $T_{AHP}$. 

B. Evolution of the AHP duration $t_e - t_i$ as a function of the slow timescale $\tau_{sAHP}$ for multiple values of the hyperpolarization level $T_{AHP}$. 

C. Duration of phase 1 $t_1$ as a function of its termination threshold $h_0$ for multiple values of the initial voltage value $h(0) = \tilde{H}_1$. 

D. End time of phase 2 $t_2$ as a function of its termination threshold $h_{AHP}$ (relatively to $T_{AHP}$) for multiple values of the hyperpolarization level $T_{AHP}$. 

E. Bursting duration as a function of $t_1$ for $\tau_{mAHP} = 0.1s$. 

F. AHP duration as a function of the threshold $\epsilon$ for $\tau_{sAHP} = 7.5s$ and $T_{AHP} = -30$. 


Figure 8: Influence of the network connectivity $J$ on bursting dynamics. A. (resp. B, C) Mean burst (resp. AHP, QP) duration in seconds from 5000s simulations for $J$ varying from 2.95 to 5.25 and three values of $K$ (left) and $L$ (right) with a fixed noise level ($\sigma = 6$).
Conclusion and discussion

We present here a novel mean-field model of synaptic short-term plasticity for the voltage, depression and facilitation variables that now accounts for long AHP periods. This model generalizes the depression-facilitation model introduced in [26] and developed in [29,30,39,40]. The AHP significantly increases the interburst duration by introducing a recovery phase after network bursting. When a Gaussian noise of small amplitude is added to the dynamics, it exhibits spontaneous bursts followed by AHP periods. We have studied here the distribution of bursts and of interbursts, decomposed in AHP and QP durations. Interestingly, we found that the distribution of bursts durations is quite concentrated (subsection 1.1). To explain this property, we studied the three-dimensional phase-space of the dynamical system (2), that contains one attractor and two saddle points. By computing numerically the two-dimensional stable manifold at one of the saddles, we found the distribution of exit points (on this manifold) when the initial point of the stochastic dynamics is located at the attractor. To compute this distribution we used two methods: 1) stochastic simulations, and 2) the method of characteristics to solve the FPE (10) in the limit of small noise. In both cases, we found a peaked distribution of exit points close to the saddle point, as predicted for two-dimensional stochastic systems [37,41,42], summarized by expression (41). After the stochastic trajectories have crossed the separatrix, they follow an almost deterministic behavior, confirming that the distribution of exit points on the separatrix defines the spread of the distribution of burst durations.

We also derived here analytical formulas (subsection 2.5) that reveal the influence of the parameters on burst and AHP durations. These computations can be used to calibrate the AHP parameters with respect to the expected values of burst and AHP durations, that could be measured experimentally. This model could thus be used to decipher the main mechanisms leading to changes in bursting and interburst dynamics, for example when the neuronal network is disrupted, during epilepsy or in the case of a glial network alteration [38].

Classical bursting models describe accurately the burst phase [4,7,9,13], but interburst is often considered as the continuation in the phase-space of the deterministic trajectories. Here the interburst phase is composed of a deterministic refractory period, the AHP, followed by the escape from an attractor due to noise (subsection 1.1). During successive bursts, trajectories are not reset at the attractor, but explore the basin of attraction. This exploration depends on the previous bursting trajectory. Thus, we expect a correlation between successive burst and interburst durations. This correlation may also depend on the amplitude of the voltage fluctuations. Finally, we predict that modifying the AHP duration could affect bursting, because it corresponds to a change in the attractor’s position and dominates the effect of synaptic depression.
A Calculation details of burst and AHP durations

A.1 Integral term of \(h\) in phase 1

To compute the integral in expression (57), we split it into two parts:

\[
\int_0^t x(s)y(s)ds = C_1 \int_0^t (A_1 e^{-\alpha_1 s} + B_1) e^{-f_1(s)} ds + \int_0^t (A_1 e^{-\alpha_1 s} + B_1) \left( \frac{1 - e^{-s f_1(s)}}{\tau_r f_1(s)} \right) ds.
\]

We start by I:

\[
I = C_1 A_1 \int_0^t e^{-\alpha_1 s - s} \left( \alpha_1 + \beta_1 + LA_1 H_1 \right) ds + C_1 B_1 \int_0^t e^{-\beta_1 s + \frac{LA_1 H_1}{\alpha_1} e^{-\alpha_1 s}} ds.
\]

Using a Taylor expansion at first order, \(e^{-\alpha_1 s} \approx 1 - \alpha_1 s\), we obtain

\[
I_A(t) \approx A_1 C_1 \int_0^t e^{-\alpha_1 s - s} \left( \alpha_1 + \beta_1 + LA_1 H_1 \right) ds \approx -\frac{A_1 \left( e^{-\alpha_1 - \alpha_1 + LA_1 H_1} - \frac{LA_1 H_1}{\alpha_1} e^{-\alpha_1 s} \right)}{\alpha_1 + \beta_1 + LA_1 H_1}
\]

and

\[
I_B(t) \approx -\frac{B_1 \left( e^{-\beta_1 + LA_1 H_1} - 1 \right)}{\beta_1 + LA_1 H_1}.
\]

Similarly, we write \(II = II_A + II_B\), where

\[
II_A(t) = \frac{A_1}{\tau_r} \int_0^t e^{-\alpha_1 s - s} \left( 1 - e^{-\beta_1 s - LA_1 H_1 e^{-\alpha_1 s}} \right) ds
\]

\[
\approx \frac{A_1}{\tau_r \beta_1} \left( \int_0^t \frac{e^{-\alpha_1 s}}{1 + \beta_1 e^{-\alpha_1 s}} ds - \int_0^t \frac{e^{-\beta_1 s}}{1 + \beta_1 e^{-\alpha_1 s}} ds \right).
\]

For (i), using the change of variable \(u = e^{-\alpha_1 s}\), we obtain

\[
(i) = -\frac{1}{\alpha_1} \int_1^{e^{-\alpha_1 t}} \frac{du}{1 + \frac{LA_1 H_1}{\beta_1} u} = -\frac{\beta_1}{\alpha_1 LA_1 H_1} \ln \left( \frac{1 + \frac{LA_1 H_1}{\beta_1} e^{-\alpha_1 t}}{1 + \frac{LA_1 H_1}{\beta_1}} \right)
\]
For small $s$, $se^{\alpha_1s} \approx s$ and using the condition $\left| \frac{LA_1H_1}{\beta_1} \right| < 1$, we expand the denominator to second order to obtain

$$(ii) \approx \int_0^t e^{-(\alpha_1 + \beta_1 + LA_1H_1)s} \left( 1 - \frac{LA_1H_1}{\beta_1} e^{-\alpha_1s} + \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-2\alpha_1s} \right) ds$$

$$\approx -\frac{e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\alpha_1 + \beta_1 + LA_1H_1} + \frac{LA_1H_1 e^{-(2\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\beta_1}$$

Finally,

$$II_A(t) \approx -\frac{1}{\tau_rLH_1\alpha_1} \ln \left( 1 + \frac{LA_1H_1 e^{-\alpha_1t}}{1 + \frac{LA_1H_1}{\beta_1}} \right) + \frac{A_1 e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\tau_r\beta_1} e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1$$

$$- \frac{LA_1H_1 e^{-(2\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\tau_r\beta_1^2} e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1 + \frac{L^2A_1^2H_1^3 e^{-(3\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\tau_r\beta_1^3} e^{-(3\alpha_1 + \beta_1 + LA_1H_1)t} - 1$$

Similarly, we obtain the following expression for

$$II_B(t) \approx \frac{B_1}{\tau_r\beta_1} \int_0^t \left( 1 - \frac{LA_1H_1}{\beta_1} e^{-\alpha_1s} + \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-2\alpha_1s} - e^{-(\alpha_1 + \beta_1 + LA_1H_1)s} \right) ds$$

$$+ \frac{LA_1H_1 e^{-(\alpha_1 + \beta_1 + LA_1H_1)s} - \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-(2\alpha_1 + \beta_1 + LA_1H_1)s} + e^{-(\beta_1 + LA_1H_1)s}}{\alpha_1}$$

Finally,

$$II_B \approx \frac{B_1}{\tau_r\beta_1} \left( t + \frac{LA_1H_1 e^{-\alpha_1t} - 1}{\alpha_1} - \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-2\alpha_1t} - 1 + \frac{e^{-(\beta_1 + LA_1H_1)t} - 1}{\beta_1 + LA_1H_1} \right)$$

$$- \frac{LA_1H_1 e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\alpha_1 + \beta_1 + LA_1H_1} + \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-(2\alpha_1 + \beta_1 + LA_1H_1)t} - 1$$

$$- \frac{LA_1H_1 e^{-(\alpha_1 + \beta_1 + LA_1H_1)t} - 1}{\alpha_1 + \beta_1 + LA_1H_1} + \left( \frac{LA_1H_1}{\beta_1} \right)^2 e^{-(2\alpha_1 + \beta_1 + LA_1H_1)t} - 1$$

### A.2 Integral term of $h$ in phase 2

Our goal is now to compute expression (59). We decompose it into four parts:

$$\int_{t_1}^t x(s)y(s) ds = I_A + I_B + II_A + II_B$$

All computations and approximations are similar except that we integrate between $t_1$ and $t$. We obtain

$$I_A(t) \approx -\frac{A_2C_2 e^{LA_2H_2}}{\alpha_2} \frac{(e^{-(\alpha_2 + \beta_2 + LA_2H_2)t} - e^{-(\alpha_2 + \beta_2 + LA_2H_2)t_1})}{\alpha_2 + \beta_2 + LA_2H_2}$$
Similarly as in phases 1 and 2 we compute the integral in expression (60) and obtain

\[ I_B(t) \approx -\frac{B_2 C_2 e^{\alpha_2}}{\alpha_2} \frac{(e^{-(\beta_2 + LA_2 H_2)t} - e^{-(\beta_2 + LA_2 H_2)t_1})}{\beta_2 + LA_2 H_2} \]

\[ II_A(t) \approx -\frac{1}{\tau_r L H_2 \alpha_2} \ln \left( 1 + \frac{LA_2 H_2 \beta}{\beta_2} e^{-\alpha_2 t} \right) \]

\[ + \frac{A_2}{\tau_r \beta_2} \frac{e^{-2(\alpha_2 + \beta_2 + LA_2 H_2)t_1} - e^{-2(\alpha_2 + \beta_2 + LA_2 H_2)t_1}}{\alpha_2 + \beta_2 + LA_2 H_2} \]

\[ - \frac{LA_2^2 H_2}{\tau_r \beta_2^2} \frac{e^{-(2\alpha_2 + \beta_2 + LA_2 H_2)t_1} - e^{-(2\alpha_2 + \beta_2 + LA_2 H_2)t_1}}{3\alpha_2 + \beta_2 + LA_1 H_2} \]

\[ II_B(t) \approx \frac{B_2}{\tau_r \beta_2} \left( t - t_1 + \frac{LA_2 H_2 e^{-\alpha_2 t} - e^{-\alpha_2 t_1}}{\alpha_2} - \frac{(LA_2 H_2)^2}{\beta_2} \frac{e^{-2\alpha_2 t} - e^{-2\alpha_2 t_1}}{2\alpha_2} \right) \]

\[ + \frac{e^{-(\beta_2 + LA_2 H_2)t_1} - e^{-(\beta_2 + LA_2 H_2)t_1}}{\beta_2 + LA_2 H_2} \]

\[ + \frac{LA_2 H_2 e^{-(\alpha_2 + \beta_2 + LA_2 H_2)t_1} - e^{-(\alpha_2 + \beta_2 + LA_2 H_2)t_1}}{\beta_2 + LA_2 H_2} \]

\[ + \left( \frac{LA_2 H_2}{\beta_2} \right)^2 \frac{e^{-(2\alpha_2 + \beta_2 + LA_2 H_2)t} - e^{-(2\alpha_2 + \beta_2 + LA_2 H_2)t_1}}{2\alpha_2 + \beta_2 + LA_2 H_2} \].

### A.3 Integral term of \( h \) in phase 3

Similarly as in phases 1 and 2 we compute the integral in expression (60) and obtain

\[ \int_{t_2}^t x(s) y(s) ds = \int_{t_2}^t (X + X(y(t_2^-) - 1)) e^{\frac{t_2 - s}{\tau_r}} + (x(t_2^-) - X) e^{\frac{t_2 - s}{\tau_f}} \]

\[ + (y(t_2^-) - 1)(x(t_2^-) - X) e^{\frac{t_2 - s}{\tau_f}} \left( \frac{1}{\tau_f} + \frac{1}{\tau_r} \right) ds \]

\[ = X(t - t_2) - \tau_r X(y(t_2^-) - 1)(e^{\frac{t_2 - t_2}{\tau_r}} - 1) - \tau_f (x(t_2^-) - X)(e^{\frac{t - t_2}{\tau_f}} - 1) \]

\[ - \frac{(y(t_2^-) - 1)(x(t_2^-) - X) \tau f \tau r}{\tau_f + \tau_r} (e^{\frac{t - t_2}{\tau_f}} - 1). \]
A.4 Numerical values of the intermediate and approximation parameters

| Parameters | Values |
|------------|--------|
| $\Gamma_1$ | -0.24  |
| $\Lambda_1$ | -0.18  |
| $\Gamma_2$ | $5.2 \times 10^{-6}$ |
| $\Lambda_2$ | 11.47  |
| $\Gamma_3$ | -0.91  |
| $\Lambda_3$ | -0.077 |
| $\Gamma_4$ | $1.4 \times 10^{-3}$ |
| $\Lambda_4$ | $4.4 \times 10^{-3}$ |
| $\Gamma_5$ | -0.99  |
| $\Lambda_5$ | 0.054  |
| $\Gamma_6$ | 0.91   |
| $\Lambda_6$ | 0.89   |
| $\Gamma_7$ | $1.9 \times 10^{-6}$ |
| $\Lambda_7$ | 0.07   |
| $\Gamma_8$ | $4.0 \times 10^{-4}$ |
| $\Lambda_8$ | $1.8 \times 10^{-3}$ |
| $\Gamma_9$ | $1.3 \times 10^{-3}$ |
| $\Lambda_9$ | $2.8 \times 10^{-3}$ |

Table 2: Intermediate parameters

| Parameters | Values |
|------------|--------|
| $H_1$     | Approximation of $h$ for $x$ and $y$ during phase 1 |
| $\tilde{H}_1$ | Initial value of $h$ |
| $H_2$     | Approximation of $h$ for $x$ and $y$ during phase 2 |
| $h_0$     | End of phase 1 threshold |
| $h_{AHP}$ | End of phase 2 threshold |
| $\epsilon$ | End of AHP threshold |
| $t_1$     | End of phase 1 time |
| $t_2$     | End of phase 2 time |
| $A_1$     | Approximation of $x$ on phase 1 parameter |
| $B_1$     | Approximation of $x$ on phase 1 parameter |
| $C_1$     | Approximation of $y$ on phase 1 parameter |
| $\alpha_1$ | Approximation of $x$ on phase 1 parameter |
| $\beta_1$ | Approximation of $y$ on phase 1 parameter |
| $A_2$     | Approximation of $x$ on phase 2 parameter |
| $B_2$     | Approximation of $x$ on phase 2 parameter |
| $C_2$     | Approximation of $y$ on phase 2 parameter |
| $\alpha_2$ | Approximation of $x$ on phase 2 parameter |
| $\beta_2$ | Approximation of $y$ on phase 2 parameter |

Table 3: Approximation parameters
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