Noise-sensitivity in bursting

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Some examples:

**Excitable dendritic spine**

Reduced membrane model for excitable dendritic spine (Wu, Baer, 1998)

FitzHugh-Nagumo kinetics for currents through the spine head membrane

Relaxation oscillation limit - $b \ll 1$

Related to FitzHugh-Rinzel model
Wu-Baer model (activity-dependent)

\[ du = (-f(u) - w - G_{ss}(u - v_s(u)) + I_{SH})dt + \delta d\beta \]
\[ dw = b(u - \gamma w) dt \]
\[ dG_{ss} = \epsilon G_{ss}(u - v_s(u)) dt \]
\[ v_s(u) = R_{SB} \frac{G_{ss} u + I_D}{1 + G_{ss}R_{SB}}, \quad f(u) = u(u-1)(u-a) \]
\[ \epsilon \ll 1, \quad \delta \ll 1 \]
Observations:

More bursts/time interval

Noise reduces lengths of silent and active phases

(Del Negro, et al., 1998)
Modeling questions:

Influence of noise vs. bifurcation parameter

\[ \delta = 0 \]
Goal:

Develop tools for extracting qualitative/quantitative information about influence of noise on transitions

Define quantities to measure sensitivity in model

Identify interactions of critical parameters and noise

Efficient computations, compared to full simulation

Parametric descriptions

Time dependent or finite time descriptions (transitions)

Limitations of “standard” measures:

Mean, Invariant density, Limiting (in time) behavior

Transitions between two different states:

Noise-dominated, crossing a Hopf bifurcation

Large relaxation oscillations + small noise
Some characteristics shared by other noise sensitive systems:

Delay bifurcations (slow variation of bifurcation parameter)

Meta-stable interfaces

Chaos with certain types of noise

Coherence resonance

Noise-driven synchronization
Wu-Baer model (activity-dependent dendritic spine)

\[
\begin{align*}
    du &= (-f(u) - w - G_{ss}(u - v_s(u)) + I_{SH}) dt + \delta d\beta \\
    dw &= b(u - \gamma w) dt \\
    dG_{ss} &= \epsilon G_{ss}(u - v_s(u)) dt \\
    v_s(u) &= R_{SB} \frac{G_{ss}u + I_D}{1 + G_{ss}R_{SB}}, \quad f(u) = u(u - 1)(u - a)
\end{align*}
\]
Transition from silent to active phase

Asymptotic approximation to the (marginal) probability density:

\[ q(u, t) = \int \int p(u, w, G_{ss}, t) \, dw \, dG_{ss} \]
Expected time of transition: Analogy to mean exit time

Relatively simple to calculate (integral of 1D probability density function)

Calculate transition time as a function of noise - full stoch simulation vs. analytical approximation

Other slow-fast transition problems\(^{(a)}\)

Reduction of chaos, (K., Papanicolaou, 1998, Physica D)

Noisy delay bifurcations (K., 1999, JSP)
Time-dependent probability density function

\[ p(u, w, G_{ss}, t) du \, dw \, dG_{ss} := \Pr((u, w, G_{ss}) \in (u + du, w + dw, G_{ss} + dG_{ss}) \text{ at time } t) \]

Fokker-Planck equation which can be derived from the system of SDE’s

\[
\begin{align*}
    d \begin{pmatrix} u \\ w \\ G_{ss} \end{pmatrix} &= \begin{pmatrix} a_1 \\ a_2 \\ a_3 \end{pmatrix} dt + \begin{pmatrix} \delta \\ 0 \\ 0 \end{pmatrix} d\beta \\
    \frac{\partial p}{\partial t} &= \delta^2 p_{uu} - \nabla \cdot (a p)
\end{align*}
\]

\[ \delta = 10^{-4}, 10^{-3}: \text{Difficulties in computations for very small diffusion} \]
Gaussian-type approximation

Deviation from deterministic behavior + WKB-type form

\[ p(u, w, G_{ss}, t) = Ce^{Q(u,w,G_{ss},t)} \]

\[ Q(u, w, G_{ss}, t) = \]

\[ - g_1(t) \frac{(u - u^d)^2}{2\delta^2} - g_2(t) \frac{(w - w^d)^2}{2\delta^2} - g_3(t) \frac{(G_{ss} - G_{ss}^d)^2}{2\delta^2} \]

\[ - h_1(t) \frac{(u - u^d)(w - w^d)}{\delta^2} - h_3(t) \frac{(u - u^d)(G_{ss} - G_{ss}^d)}{\delta^2} \]

\[ - h_3(t) \frac{(w - w^d)(G_{ss} - G_{ss}^d)}{\delta^2} + q_1(t) \frac{u - u^d}{\delta} \]

\[ + q_2(t) \frac{w - w^d}{\delta} + q_3(t) \frac{G_{ss} - G_{ss}^d}{\delta} + s(t) \]
System of ODE's:

\[-\frac{\dot{g}_1}{2} = g_1 d_1^{(1)} + g_1^2 + d_1^{(1)} h_{12} + d_2^{(1)} h_{13}\]

\[-\frac{\dot{g}_2}{2} = g_2 d_2^{(2)} + g_1^2 + d_2^{(1)} h_{12} + d_3^{(1)} h_{23}\]

\[-\frac{\dot{g}_3}{2} = g_3 d_3^{(3)} + g_2^2 + d_1^{(1)} h_{13} + d_2^{(3)} h_{23}\]

\[-\dot{h}_{12} = 2g_1 h_{12} + h_{12} d_1^{(1)} g_1 d_1^{(2)} + h_{12} d_2^{(2)} + g_2 d_1^{(1)} + h_{13} d_2^{(3)} + h_{23} d_3^{(1)}\]

\[-\dot{h}_{13} = 2g_1 h_{13} + h_{13} d_1^{(1)} g_1 d_3^{(3)} + h_{13} d_3^{(3)} + g_3 d_2^{(1)} + h_{12} d_2^{(3)} + h_{23} d_2^{(1)}\]

\[-\dot{h}_{13} = 2h_{12} h_{13} + h_{23} d_3^{(3)} + g_3 d_2^{(2)} + h_{23} d_2^{(2)} + g_2 d_3^{(3)} + h_{12} d_1^{(3)} + h_{13} d_1^{(2)}\]

\[-\dot{q}_1 = -2g_1 q_1 - q_1 d_1^{(1)} - q_2 d_2^{(1)} - q_3 d_3^{(1)}\]

\[-\dot{q}_2 = -2h_{12} q_1 - q_1 d_1^{(2)} - q_2 d_2^{(2)} - q_3 d_3^{(2)}\]

\[-\dot{q}_3 = -2h_{13} q_1 - q_1 d_1^{(3)} - q_2 d_2^{(3)} - q_3 d_3^{(3)}\]

\[\dot{s} = q_1^2 - d_1 y_1 - d_2 y_2 - d_3 y_3 - g_1\]

\[d_j^{(m)} = \frac{\partial d_j}{\partial y_m}, \ m = 1, 2, 3.\]
End of active phase

Multiscale analysis for end of active phase: Slowly varying modulation to oscillations $T = \epsilon t$

$$u = U(t + \phi(T)) + \epsilon A(T)W(t + \phi(T))$$

$U$, $W$ gives the limit cycle for $u$, $w$ with $G_{ss}$ constant

Slow SDE’s give reduction of active phase
Transition out of the active phase:

Look for multiscale (averaged) equations

Identify slow variables - slow time $T = \epsilon t$:

$dG_{ss} = \epsilon G_{ss}(u - v_s(u)), \quad (z(T) = \langle G_{ss}(t) \rangle)$

$u(t) = U(t + \theta(T)) + \epsilon A(T)W'(t + \theta(T))$

$w(t) = W(t) - \epsilon A(T)U'(t + \theta(T))$

$(U, W)$ is the limit cycle for fixed $G_{ss}$ (Neu, 1980)

Look for equations for $A(T), \theta(T)$:

$$dA = \psi_A(A, \theta, z(T))dT + \sigma_A d\zeta_1(T)$$

$$d\theta = \psi_\theta(A, \theta, z(T))dT + \sigma_\theta d\zeta_2(T)$$

Derive equations for $\psi, \sigma$
Ito’s formula:

\[ du = \left[ U'(t + \theta(T)) + A(T)W''(t + \theta(T)) \right. \]
\[ \left. \psi_A \frac{\partial u}{\partial A} + \psi_{\theta} \frac{\partial u}{\partial \theta} + \frac{1}{2} \sigma_{\theta}^2 \frac{\partial^2 u}{\partial \theta^2} \right] dt \]
\[ + \sigma_A \frac{\partial u}{\partial A} d\zeta_1 + \sigma_{\theta} \frac{\partial u}{\partial \theta} d\zeta_2 \]

Substitution in equation for \( u \):

\[ du = \left[ -f(U) - W - f'(U)A(T)W' + A(T)U' \right. \]
\[ \left. - z(T) \left( U + -v_s(U)A(T)W' - v'_s(U)A(T)W' \right) \right] \]
\[ + \delta d\beta \]

Similarly for \( w \)

Consider \( W' du - U' dw, \ U' du + W' dw \)
\[(U'^2 + W'^2)\psi_\theta dT = \epsilon A(T) \left[-U'W'f'(U) + (W')^2\right] dt + O(\epsilon^2)\]

Treat \(\epsilon dt = dT, A(T), \theta(T)\) as constants.

Average over period of \(U\) and \(W\)

\[\psi_\theta = \frac{H_1(U, W)}{H_2(U, W)} A(T) \equiv h_5 A(T)\]

Similarly for \(\psi_A, \sigma_A, \text{ and } \sigma_\theta\)

**Multi-scale:** Different time scales \(T\) and \(t\) treated as independent.

Functions of \(T\) treated as independent of \(t\)

(Method of averaging)

Similar for \(\beta(t) = \frac{1}{\epsilon} \left[U(t)\zeta_1(T) + W(t)\zeta_2(T) + \Sigma_j \zeta_j(T)\Phi_j(t)\right]\)

Terms with \(\Phi_j\) decay: \(U, W\) attractor

Multi-scale assumption: Small/slow effect of noise over long time scale
System of equations for $A$, $\theta$ and $z$ (Neglecting $O(\epsilon^2)$ terms)

$$
\begin{align*}
\frac{dA}{dT} &= (h_1 A + h_2 z A + \frac{\delta^2}{\epsilon} h_3) dT + \frac{\delta}{\sqrt{\epsilon}} h_7 d\zeta_1(T) \\
\frac{d\theta}{dT} &= h_5 A dT + \frac{\delta}{\sqrt{\epsilon}} h_6 d\zeta_2 \\
\frac{dz}{dT} &= z(U - v_s(U)) dT
\end{align*}
$$

Gives deviation from periodic behavior (amplitude and phase)

Average increase in $G_{ss}$
Quantitative measures of the effect of noise

Computational efficiency: Analytical approximations
Fast computations over long time scales, using multi-scale analysis
Critical scalings between parameters to indicate "effective" noise influence
Asymptotic method to quantitatively measure effect of noise on transitions

Asymptotic approximations for deviations from deterministic dynamics: FPE

Transitions from near steady state to oscillations

Multi-scale/averaging/projection method: Separate regular oscillations from noise

Transitions from large oscillations to approach of steady-state

Effective noise scalings

Fast simulations of reduced problems
Noise induced synchrony in networks:

Optimal noise levels for synchronized transitions to active states


Multiscale dynamics: noise significant in transitions
Epidemics: Stochastic vs. Deterministic SIR models

Susceptible $\rightarrow$ Infected $\rightarrow$ Recovered

Observations and Monte Carlo simulations:
Significant oscillations following spike in infected populations

Deterministic models: Damping of spikes $\rightarrow$ steady-states

Models for stochastic modulations of “regular”oscillations: age, demographic information
Criteria for coherence resonance: multi-scale stochastic sustained oscillations in the infected population

Boundaries in the $R_0 - \gamma$: Secondary infection rate vs. recovering parameter

(K., Greenwood, Gordillo, 2006)