Phenomenological network models: lessons for epilepsy surgery

Supplementary material 1: Detailed model description

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1 Detailed model description

Following [1, 2, 4], we consider a phenomenological model of inter-ictal and ictal dynamics. This model consists of nodes coupled through a directed graph. The dynamics of node k is described by two variables: a complex activity variable z_k and a real variable λ_k that represents the excitability of the node. The observable quantity for each node is the real part of z_k, representing an EEG signal. Each node can produce two types of activity: noisy low-amplitude inter-ictal activity and pronounced oscillations that represent ictal activity.

We will interpret these two activity types in terms of dynamical system properties by considering the dynamics of a single node as a slow-fast system. Studying the node dynamics as a slow-fast system is allowed since changes in the excitability λ_k are slow compared to z_k. First we look at the dynamics of the fast system, i.e. the dynamics of z_k for fixed λ_k. In this system, inter-ictal activity arises from noisy perturbations around a stable equilibrium, while ictal activity is generated by a stable limit cycle. Figure 1 shows a bifurcation diagram of the fast system. Here one can see that for $\lambda_k < 1$ the fast system has a stable equilibrium at $z = 0$, which is indicated by the solid blue line. At $\lambda_k = 1$ a Hopf bifurcation occurs and the equilibrium becomes unstable for larger values of λ_k (dashed blue line). From the Hopf bifurcation an unstable limit cycle emerges. This unstable limit cycle exists for $0 < \lambda < 1$. At $\lambda = 0$, this unstable limit cycle changes via a limit point of cycles (LPC) bifurcation to a stable limit cycle. This stable limit cycle exists for $\lambda_k > 0$. Both the unstable and stable limit cycle are a circle centered around $z = 0$ in the complex plane. Their radii are indicated by the green line in the bifurcation diagram in Figure 1. The frequency of the limit cycles is determined by a parameter ω. In this study we set $\omega = 20$. This yields a frequency of around 3 Hz, comparable to the frequency of spike-wave discharges.

The speed of the slow dynamics is regulated by a time constant τ. Motivated by the experimental work of [3], we choose $\tau = 5$ s. If the fast system is in inter-ictal state, the slow dynamics will try to move λ_k towards $\lambda_{0,k}$. Therefore $\lambda_{0,k}$ can be seen as the base level of excitability. In this study we take $\lambda_{0,k} = 0.6$ for a normal node and $\lambda_{0,k} = 0.65$ for a more excitable node. For these values of $\lambda_{0,k}$, the system has a stable equilibrium at $z = 0$ and $\lambda_k = \lambda_{0,k}$.

An important aspect in this model is that each node receives independent white noise input with strength α representing background input from unmodeled brain regions. In this study we take $\alpha = 0.1$. The noise perturbs the system around the stable equilibrium state. This is visible as the noisy perturbations seen in the inter-ictal activity. However, if $0 < \lambda_{0,k} < 1$, the noisy input may force z to jump to the stable limit cycle, representing the ictal activity. As a reaction λ_k will slowly decrease. During this process the fast z_k activity will adapt immediately. When λ_k gets smaller than zero, the stable limit cycle of the fast dynamics disappears and the fast system jumps back to the inter-ictal state. At this moment the slow λ_k will increase again to the base level $\lambda_{0,k}$. In the left plot in Figure 1 an example of a transition from inter-ictal to ictal activity and the subsequent transition to inter-ictal activity is indicated in the λ_k-$|z_k|$-plane by the red line. The corresponding time series for the output variable $\mathrm{Re}(z_k)$ and the excitability λ_k are shown in the right plots.

We note that when the system is in inter-ictal state and λ_k is at its resting value, then the escape time from inter-ictal activity to ictal activity is stochastic and approximately exponentially distributed [1]. This escape

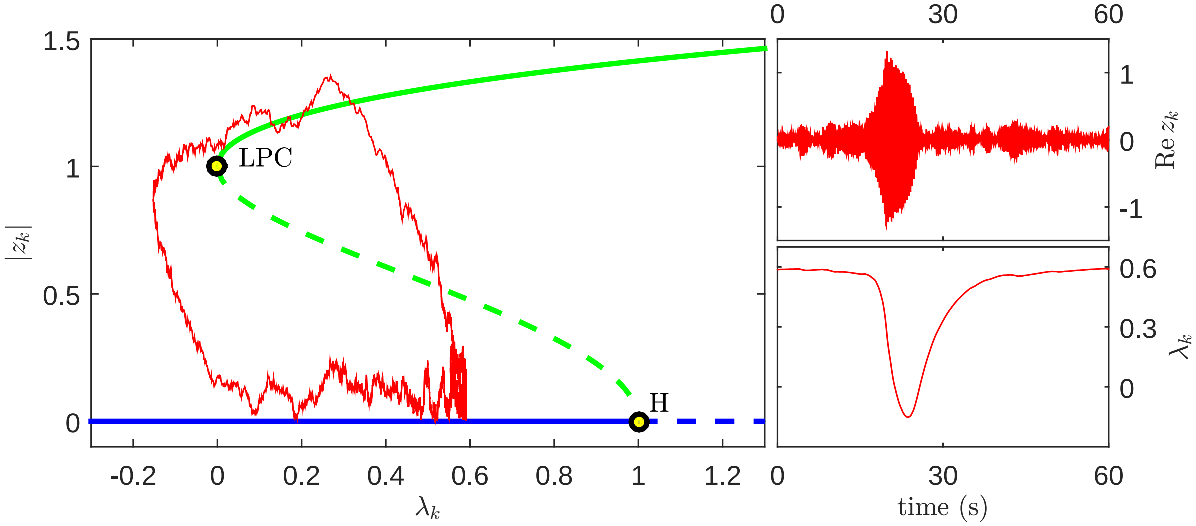

Figure 1: Left: Bifurcation diagram for $|z_k|$ as function of λ_k. The blue line indicates the equilibrium $z = 0$. The green line indicate the limit cycle. Solid lines are stable solutions, dashed lines are unstable solutions. The red line shows variation of $|z_k|$ and λ_k during a transition from inter-ictal to ictal activity and back to inter-ictal activity. The plots on the right display $\mathrm{Re}\,(z_k)$ and λ_k against time for this situation.

time decreases if the base level of excitation $\lambda_{0,k}$ or the noise strength α is increased [1]. The duration of an episode of ictal activity is approximately deterministic of length, since this depends mainly on the slow process and its time constant τ. The same holds for the time needed to get back from low excitation level to the base level excitation after an episode of ictal activity.

Besides background input, each node also receives input from other nodes. This input is modeled as diffusive coupling on a simple directed graph, which means that it influences the activity of the receiving node to move towards the activity of the projecting node. The directed graph can be described by an adjacency matrix M. In this matrix $\mathrm{M}_{kl} = 1$ if there is a connection from node l to node k (and thus node k receives input from node l) and $\mathrm{M}_{kl} = 0$ if there is no connection. We exclude self-connections, so $\mathrm{M}_{kk} = 0$ for all k, since we assume that the influence of self-connections can be represented by the intrinsic dynamics of a node. The strength of all connections is given by a global constant β. In this study we set $\beta = 0.4$.

The description above leads to the following set of Itô-type stochastic differential equations:

$$\begin{aligned}
\mathrm{d}z_k &= \left(z_k \left(\lambda_k - 1 + i\omega + 2\left|z_k\right|^2 - \left|z_k\right|^4 \right) + \beta \sum_{l=1}^{4} M_{kl}(z_l - z_k) \right) \mathrm{d}t + \alpha \mathrm{d}W_k, \\
\tau \mathrm{d}\lambda_k &= \left(\lambda_{0,k} - \lambda - |z_k|^2 \right) \mathrm{d}t,
\end{aligned}$$

where the nodes are numbered $k = 1, \ldots, 4$. We compute solutions to this system of stochastic differential equations using an Euler-Maruyama scheme with time steps of 0.0001 seconds.

References

[1] O. Benjamin, T. H. B. Fitzgerald, P. Ashwin, K. Tsaneva-Atanasova, F. Chowdhury, M. P. Richardson, and J. R. Terry. “A phenomenological model of seizure initiation suggests network structure may explain seizure frequency in idiopathic generalised epilepsy”. *Journal of Mathematical Neuroscience* 2.1 (2012), pp. 1–41.

[2] S. N. Kalitzin, D. N. Velis, and F. H. Lopes da Silva. “Stimulation-based anticipation and control of state transitions in the epileptic brain”. *Epilepsy and Behavior* 17.3 (2010), pp. 310–323.

[3] P. Suffczynski, F. H. Lopes Da Silva, J. Parra, D. N. Velis, B. M. Bouwman, C. M. Van Rijn, P. Van Hese, P. Boon, H. Khosravani, M. Derchansky, P. Carlen, and S. Kalitzin. “Dynamics of epileptic phenomena determined from statistics of ictal transitions”. *IEEE Transactions on Biomedical Engineering* 53.3 (2006), pp. 524–532.

[4] J. R. Terry, O. Benjamin, and M. P. Richardson. “Seizure generation: The role of nodes and networks”. *Epilepsia* 53.9 (2012), e166–e169.