Noise-driven *up-down* transitions in a simple model for general anesthesia

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A characteristic pattern with sequences of alternating quiescent (down) and bursting (up) states of activity can be observed in neuronal recordings during deep sedation induced by general anesthesia [1, 2]. Prevailing models suggest that such bi-stable dynamics might be explained by frequent noise-induced transitions between two stable (attracting) branches. However, the mathematical tractability of these non-linear scenarios is limited by its high dimensionality and exact solutions to these problems are only known for 1D systems. Here, the 2D neural mass model proposed in [3] is studied. The model describes the dynamical evolution of the excitatory (V_e) and inhibitory (V_i) PSPs on a target neuron under the action of *propofol*, an anesthetic drug of frequent clinical use. Firstly, approximate expressions for the eigenvalues are derived, that consistently permits to classify the kind of fixed points in most of the cases, broadening so the analysis presented in [3]. It is found that stable nodes might bifurcate to unstable fixed points or stable foci only when the effective membrane potential $V_m = V_e - V_i$ decreases to values in the vicinity of the spiking excitatory threshold. The analysis would help replicate experimental facts already reported in general anesthesia, such as typical peaks in the EEG spectrum. For instance, it is shown that stable foci can only be considered when the excitatory and inhibitory threshold values are approximately equal.

In a second analysis, neuronal firing rates are modeled with a Heaviside function, instead of a Sigmoid as originally done in [3], with no essential modifications of the phase-portraits. This allows the 2D domain to be split into two semi-infinite regions, with one attraction basins each and whose deterministic dynamics can be (locally) described by gradient functions, what makes a link to solvable systems (see Fig. 1). Besides, mathematical expressions for the value of the membrane potential ($\overline{V}_m$) as well as both coordinates ($\overline{V}_e$ and $\overline{V}_i$) at the fixed points can be derived. In addition, the related bifurcation diagrams are obtained by using analytical expression of the nullclines and their intersections (the fixed points). The expressions make explicit the dependence of the model dynamics on the propofol level and the adequate parametric ranges to obtain bi-stability.

Finally, the mathematical formulation of the random 'switching' process between the two attractors, in terms of first-passage time theory [4], is presented. By means of sample (noise-free) trajectories plotted in the phase portraits containing the attractors, the exit boundary is identified: the *separatrix* delineating the two attraction basins. The possibility to reduce the escape problem to just *one* exit point is also discussed, what is related with point-like exchange probability currents in clear analogy to 1D systems. These conjectures are supported by numerical results.

References

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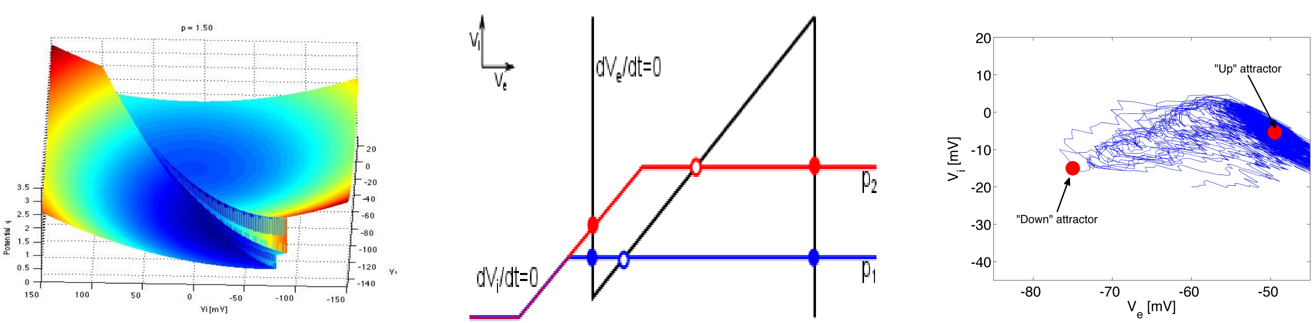

Figure 1: The Heaviside variant of the model proposed in [3], with noise-induced switches between two stable nodes. Left: the deterministic evolution at each attraction basin locally obeys a gradient dynamics as in 1D systems. Center: a sketch showing the V_e and V_i nullclines and their interceptions (fixed points) for increasing values p_1 (in blue) and p_2 (in red) of the anesthesia level. Filled circles represent the 'up' and the 'down' attractors located on the right and on the left, respectively, of a unique saddle (empty circle). Right: a sample trajectory generated by the whole system's dynamics, with continuous excursions between the 'up' and 'down' attractors.