AN EVOLUTIONARY APPROCH TO THE SEARCH FOR PERIODIC AND CHAOTIC OSCILLATIONS IN HODGKIN-HUXLEY MODEL

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This work presents an analysis of the original Hodgkin-Huxley (HH) model in a non-smooth (rectangular pulses) excitation scenario and also a method to search for specific oscillating patterns in this dynamical system. The analysis is based on a classical qualitative method given by the bifurcation diagram and on the calculation of the system Lyapunov spectrum. This calculation was carried out by means of a modified algorithm particularly suited to deal with the non-smoothness and complexity of the state equations. The obtained Lyapunov exponents are then used to build a cost function for seeking pre-defined dynamical patterns that is optimized using the particle swarm optimization algorithm.

In [1] and [2], Soriano *et al.* proposed and tested a method (called cloned dynamics - ClDyn) to perform the analysis of the stability of dynamical systems by calculating their Lyapunov spectrum without the need for a linearization process, which is particularly attractive for dynamics with a complex mathematical description and/or discontinuous inputs. In simple terms, the ClDyn approach is based on the idea of analyzing the evolution of difference state vectors defined as the distance from the original (fiducial) trajectory and the clones of the motion equations initially disturbed by small values in orthogonal directions. The whole system, which comprises the original motion equations and the clones, is numerically integrated for a brief interval, and then the different state vectors are updated and corrected by using the same correcting procedure present in the classical method to perform Lyapunov spectrum calculation, the Gram-Schmidt Reorthonormalization (GSR) [3]. The local divergence (or convergence) is computed to evaluate the local Lyapunov spectrum, and, finally, the clones are displaced in the neighborhood of the fiducial trajectory to restart the integration procedure, which defines an iteration of the algorithm. The whole procedure stops only when a representative number of iteration captures the average divergence rate of initially close trajectories in the phase space for the whole attractor. Details can be found in [1] and [4].

Using this approach, the Lyapunov spectrum of the emblematic HH model was calculated under the excitation of a rectangular train of pulses, a situation closer to the canonical experimental procedures, or, at least, closer to the mathematical representation of experiments. In fact, action potentials are commonly evoked by abrupt stimulation (e.g. step currents or rectangular pulses) as usually employed in patch clamp experiments and in experiments to evaluate the refractory period or to obtain the strength vs. duration curve for excitable cells [5, 6].
Figure 1 shows the bifurcation diagram and largest Lyapunov exponent (λ_1) obtained for the original HH model under excitation of a rectangular train of pulses taking the amplitude (A) of excitation as control parameter and fixing its period (T) in 7 ms with duty cycle of 50 %.

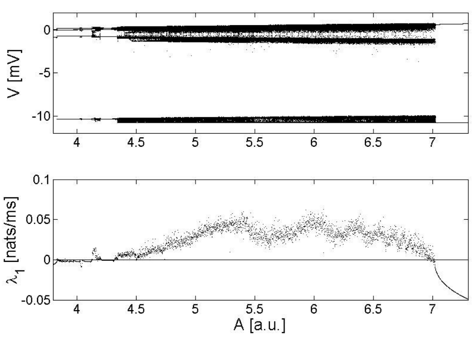

Figure 1: The upper panel shows the bifurcation diagram built by sampling the membrane potential V every time that m = 0.05 taking A as control parameter with a step size of 10^{-4}. The lower panel shows the λ_1 for the same range of A with step size of $2.5\cdot10^{-4}$.

As chaotic systems exhibit at least one positive Lyapunov exponent, the lower panel of Figure 1 reveals the presence of chaos in the HH model for a significant range of A, which is in perfectly agreement with the qualitative behavior captured by the bifurcation diagram (upper panel). Moreover, after exposing the wealth of dynamical behaviors in this neuronal model, it becomes possible to seek for specific oscillating patterns by defining a reference Lyapunov spectrum on a cost function that can be minimized under different model parameters. For instance, Eq. (1) describes a cost function to be optimized under the membrane (sodium and potassium, respectively, G_{Na} and G_K) conductance parameters:

$$f(G_{Na}, G_K) = \sum_{i=1}^{n} \sqrt{\left(\lambda_i - \hat{\lambda}_i(G_{Na}, G_K)\right)^2} \qquad (1)$$

where λ_i, $i = 1, \ldots, n$ are the reference Lyapunov exponents, $\hat{\lambda}_i$, $i = 1, \ldots, n$ are the estimated Lyapunov exponents. Let us take, as an illustration, the Lyapunov spectrum for the original HH model (which implies $G_K = 36$ and $G_{Na} = 120$ mS/cm^2) and $A = 6$ as a reference. It is possible to change A from 6 to 7.3 (which would turn the chaotic behavior into that of a limit cycle, as can be seen in Figure 1) without changing the chaotic oscillating characteristics if the model parameters G_K and G_{Na} are changed in order to minimize the cost function defined in Eq. (1). As the surface defined by this equation is highly multimodal, an alternative method to perform the optimization is required, since the derivatives required by classical gradient-based approaches would be quite difficult to obtain and these approaches are not particularly suited to perform global search. In this case, we decided to employ a bio-inspired optimization method known as particle swarm [7], which possesses a significant global search potential and does not require cost function manipulations.

The upper panel in Figure 2 shows the reference time series obtained for $A = 6$, $G_K = 36$ and $G_{Na} = 120$, and the time series obtained by using the parameters G_K and G_{Na} found by the optimization algorithm when A is changed to 7.3. It can be noted that the effect on the oscillating pattern that would be generated by the change in A can be compensated by the change in conductance parameters. Obviously, as both systems are chaotic, the time series are not identical, but they have similar statistical properties (probability distribution, mean, standard variation), and, more than that, are very close in the phase space (lower panel – Figure 2), something that can be very useful for control purposes.

Using this approach, not only periodic orbits can be degenerated into chaotic behavior changing the membrane characteristics, but also chaotic trajectories can be stabilized into periodic oscillations. This occurs, for instance, when we take the reference Lyapunov spectrum produced when $A = 7.3$, $G_K = 36$, $G_{Na} = 120$ (that leads to a limit cycle), and optimize the systems under $A = 6$ (which implies in a chaotic behavior for the original HH parameters) to achieve the desired periodic oscillation by changing membrane characteristics to $G_K = 30.3$ and $G_{Na} = 128.9$.

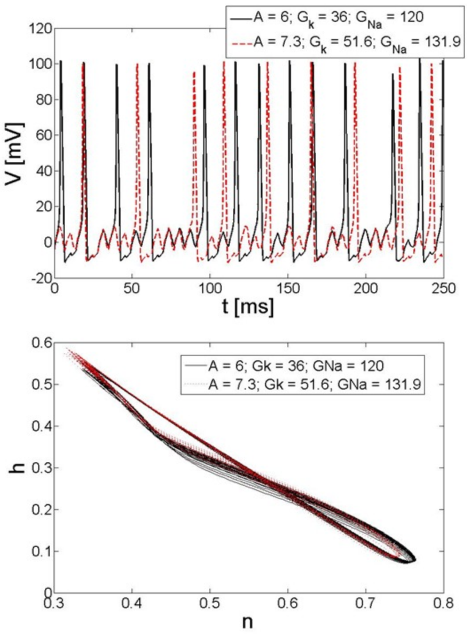

Figure 2: The upper panel shows the reference time series obtained when ($A = 6$, $G_K = 36$, $G_{Na} = 120$) and the time series obtained after setting the conductance parameters by the optimization process when $A = 7.3$. The lower panel shows the phase portrait for h and n state variables for the reference and obtained solutions.

In simple terms, it can be said that the central contribution of this line of research is to present means to analyze and seek for specific oscillating patterns avoiding the manipulation (e.g. differentiation) of the state equations, which was done by modifying the classical way to perform the Lyapunov spectrum calculation, and by the use of a bio-inspired metaheuristic method.

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