Wavenet identification and input estimation from single voltatge traces

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OUTLINE

- We present a computational procedure both to obtain a heuristic neuron model and to estimate input parameters from single voltage traces.
- The procedure is based on an efficient use of artificial neural networks (ANN) built on wavelets (*wavenet*). More precisely, a modification of wavenets aiming at decreasing the number of functions used[1].
- We identify (obtain a black-box *synthetic* equivalent model) by means of the wavenet.
- By computing the inverse wavenet, we are able to provide input estimations from voltages traces and further distinguish between excitatory and inhibitory input conductances.
- We test our procedure with the Morris-Lecar model as a proof-of-concept instantiated by conductance-based neuron models, but it has potential applications to experimental data.

MODEL

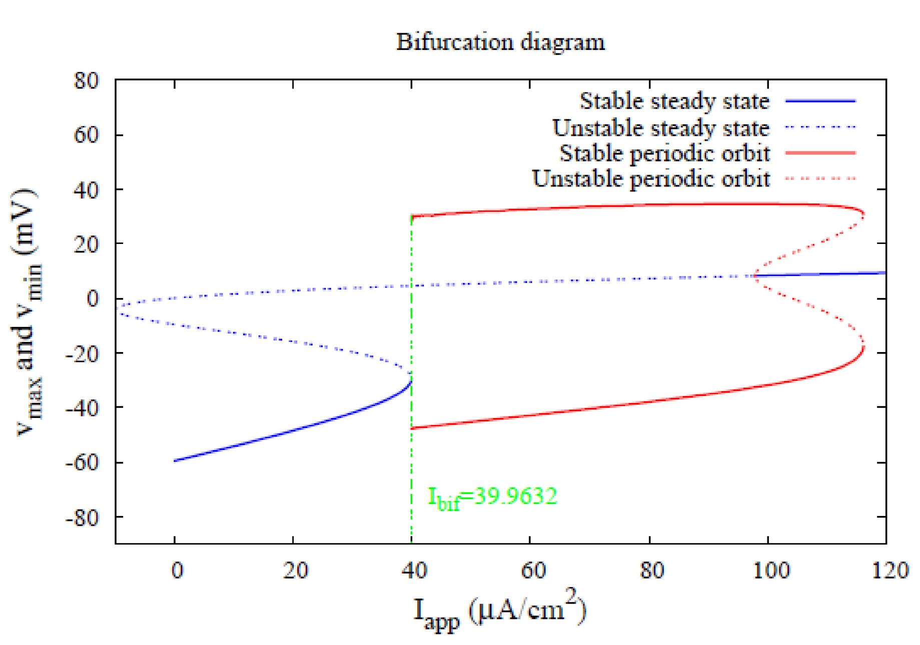
We consider the Morris-Lecar model:

$$C\frac{dv}{dt} = -g_L(v-E_L) - g_K\, w\,(v-E_K) - g_{Ca}\, m_\infty(v)\,(v-E_{Ca}) + I, \quad (1)$$

$$\frac{dw}{dt} = \phi\frac{w_\infty(v)-w}{\tau_w(v)}, \quad (2)$$

$E_L = -60$, $E_K = -84$, $E_{Ca} = 120$ (mV)
$V_1 = -1.2$, $V_2 = 18$, $V_3 = 12$, $V_4 = 17.4$ (mV)
$g_L = 2$, $g_K = 8.0$, $g_{Ca} = 4.0$ (mS/cm^2).

Ultimate goal: **estimating the input $I = I_{app} + I_{syn}$ from the voltage traces.**



Bifurcation diagram of system (1-2) in terms of $I =: I_{app}$.

FUNCTION APPROXIMATION USING WAVELETS THEORY

Wavelets form a family of functions, constructed from expansions and translations of a basic function $\Psi(.)$ called *wavelet mother* (here, a quadratic spline).

$$\Psi_{(a,b)}(t) = |a|^{-1/2}\Psi\left(\frac{t-b}{a}\right).$$

A standard particular choice (*discrete wavelets family*) is:

$$\Psi_{(m,n)}(t) = |a_0|^{-m/2}\Psi\,(a_0^m t - nb_0)\,;\, m,n \in Z.$$

They can represent any function $f(t) \in L^2(R)$:

$$f(t) = \sum_m\sum_n c_{m,n}\Psi_{m.n}$$

Series expansion is generally divided into 2 parts: non-refined information identified by an expansion in scaling functions $\Phi_{0,n}$ (quadratic spline) and details identified by wavelets $\Psi_{m,n}$. The complete signal is the sum of both parts:

$$f(t) = \sum_{n=-\infty}^{n=\infty} d_n\Phi_{0,n}(t) + \sum_{m=0}^{m=\infty}\sum_{n=-\infty}^{n=\infty} c_{m,n}\Psi_{m,n}(t)$$

Modified wavenet

The proposed modification combines localized and global scaling functions unlike classical Wavenets, which only use localized wavelets and scale functions.

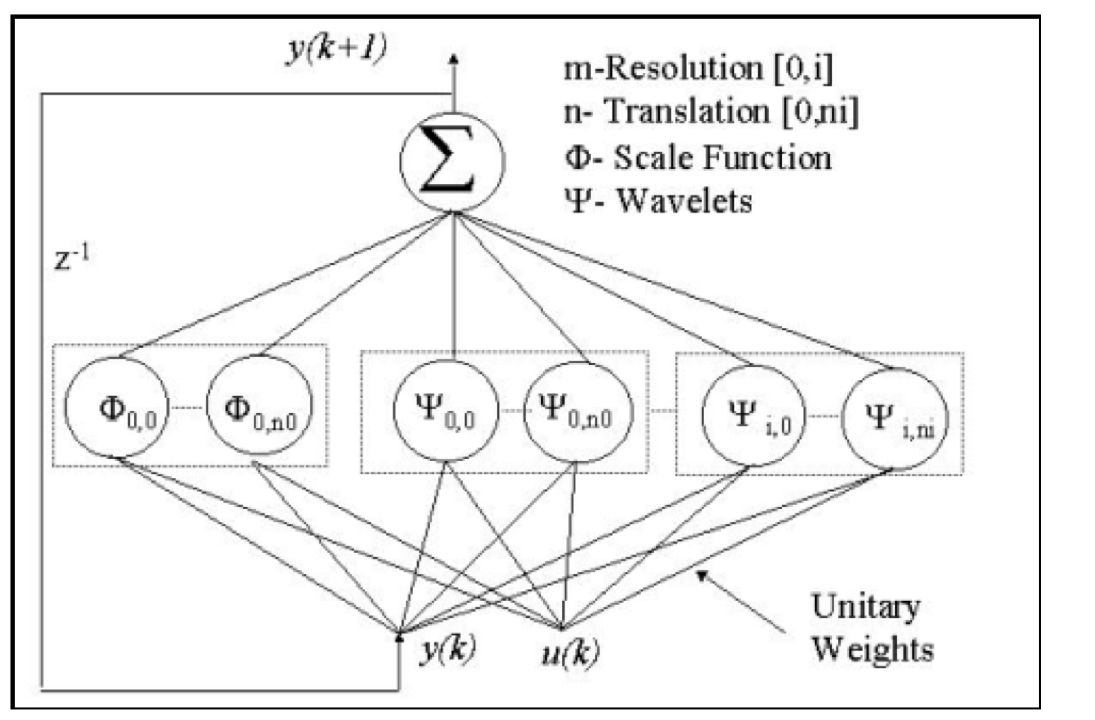
Network structure

Network has a single output, $\mathbf{y(k+1)}$, the predicted variable at time $(k+1)$. and two inputs: the perturbation variable (exogenous) $\mathbf{u(k)}$ and the current output $\mathbf{y(k)}$ (see figure). The weights of input layer are taken as 1.

Dynamical systems identification

The identification of a dynamical system consists of:

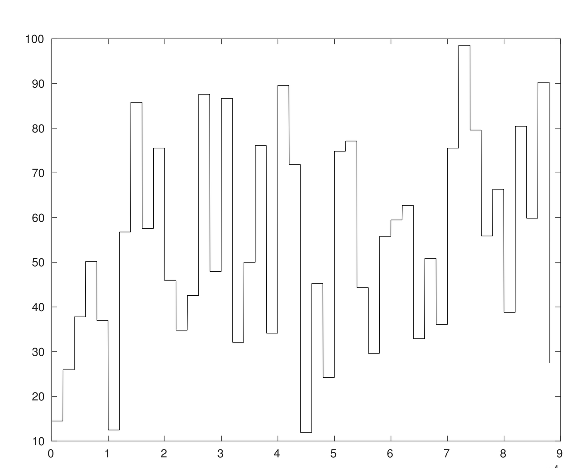
1. Acquisition of data groups for fitting (training patterns): data obtained by solving the system of differential equations.
2. Determination of the best network structure: Studying what set of input variables better identifies the process. Simple criterion: the smaller number of variables giving the smallest quadratic error.
3. Simulation: Acquisition of a new data group (test), relating inputs to outputs, different from that used in training. The network performance is evaluated in relation to test data group (crossed validation).
4. Validation through dynamic prediction. In this case, the first point of the validation data group (initial condition) is used as an input to the network. In relation to the other points, only the information of perturbation variable is used, as external information, and a feedback of the output variables is made.



IDENTIFICATION OF THE ML MODEL

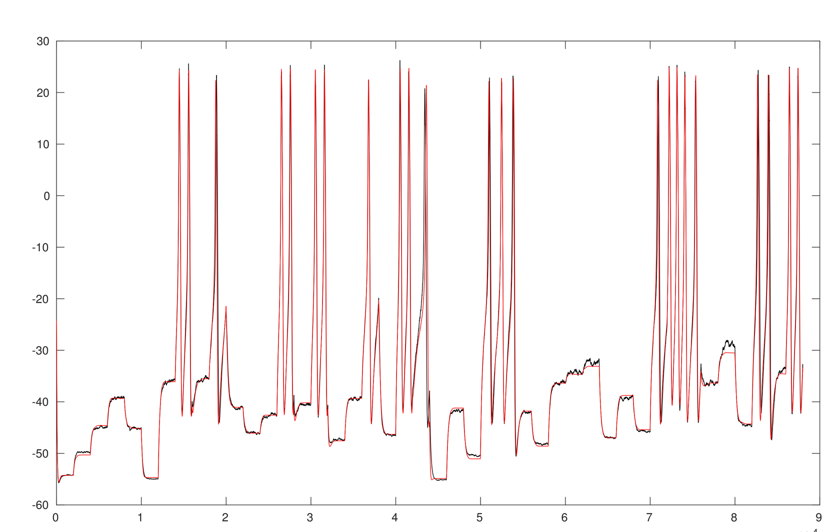
Inputs (5): $I_{app}(t)$, $v(t-h)$, $w(t-h)$, $v(t-2h)$, $w(t-2h)$.
Network: 1 level of activation functions; $\rho = 1e-7$

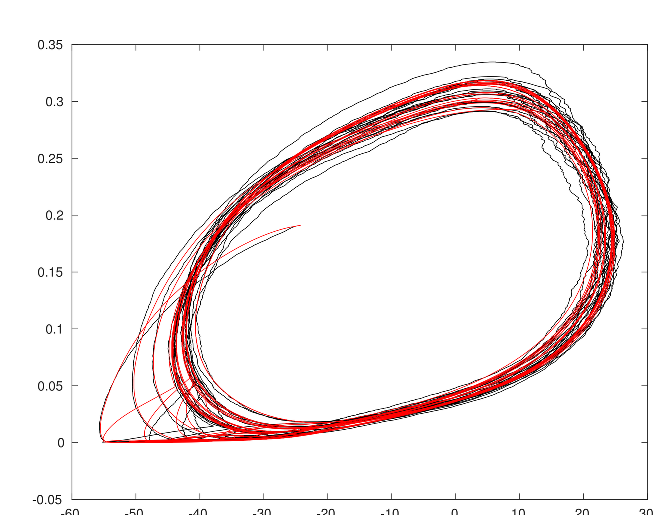
(ρ = regularization parameter, composed by the quadratic error of the output and the weights of the network squared to penalize the excessive curvatura of the surface).



Injected current trace, $I_{app}(t)$ (50 levels uniformly distributed, sample frequency 20 000 Hz).

Outputs (2): $v(t)$, $w(t)$.





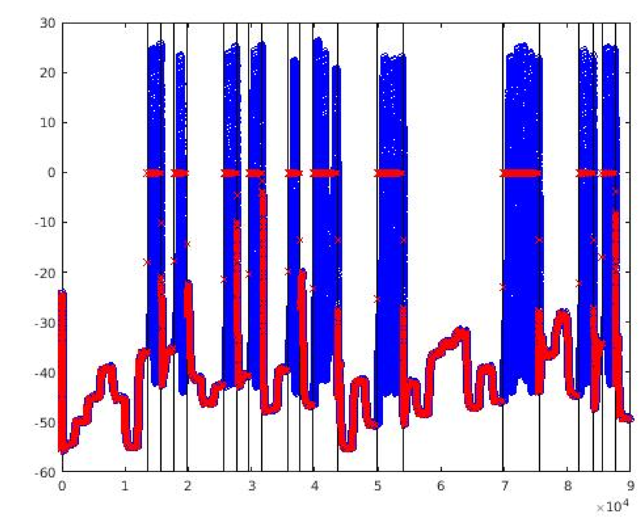
In **red**, simulation from the ML model; in **black**, the output from the wavenet network.

Voltage trace $v(t)$ (above) and phase portrait on $v-w$ plane (below).

Notice the excellent match of the wavenet simulation compared to the simulation of the system of differential equations.

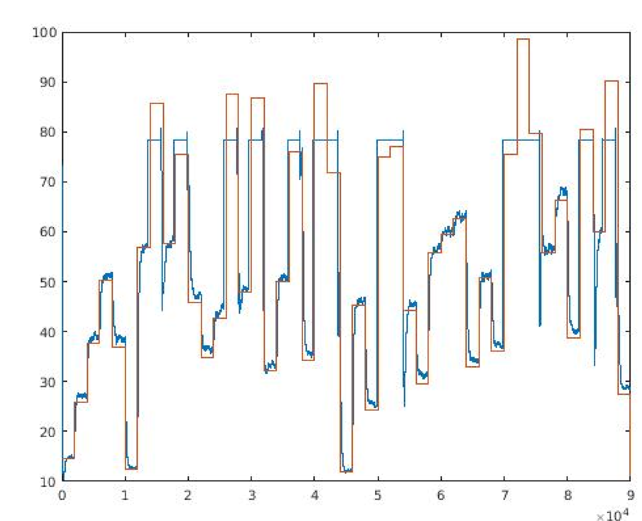
INVERSE WAVENET: INPUT ESTIMATION

- We perform the inverse prediction, using an inverse wavenet that provides currents from voltages. Using the original $I_{app}(t)$ current as the target, we train the inverse network.
- We use the voltage trace to obtain $I_{estim}(t)$, the estimated input current, from the inverse wavenet.
- Technical issue: to avoid oscillations in suprathreshold estimations, a mask was generated to separate subthreshold from suprathreshold.
- To verify the quality of the current estimation, the estimated current I_{estim} is then used as the input of the direct network.



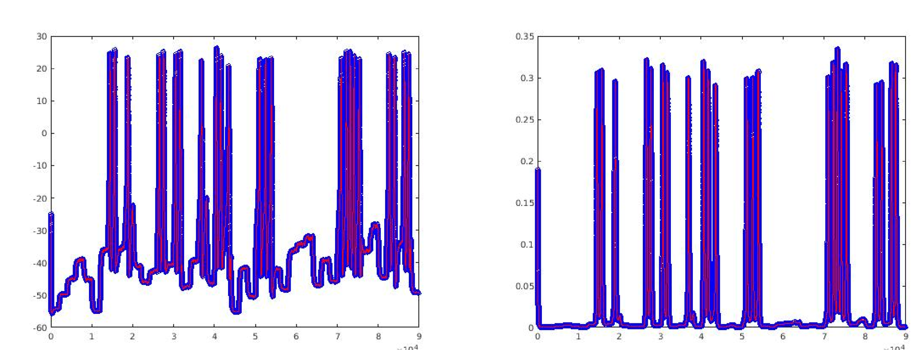
In **blue**, the original v-output; in **red**, the masked output v_{mask}.

Voltage processed with **mask** (in **black**).



The estimated input current $I_{estim}(t)$ is shown in green; in ochre, the original $I(t)$.

Estimated currents using the inverse neural network.



Verification of the quality of the current estimation. The estimated current I_{estim} is used as the input of the direct network, obtaining the traces of the voltage $v(t)$ and the gating variable $w(t)$, in **red**. In **blue**, the voltage v and gating variable w obtained by using a trained network with original input.

CONCLUSIONS

1. Identification: From an appropriately designed input and the corresponding voltage trace, we obtain a black-box model the ANN identifies the neuron's behaviour with high accuracy. Interestingly, the interval of input currents used to train the wavenet includes both quiescent and spiking regimes, thus tracking also abrupt changes in the bifurcation diagram.
2. Estimation: We also show how the wavenet methodology can also be applied to the reverse situation, that is, to provide input estimations from voltage traces (inverse wavenets). Estimating the synaptic input (synaptic conductances) is the ultimate goal, an active research problem line with no complete solutions yet, see for instance [2].
3. Similar results obtained for more realistic conductance-based models (not shown here). Tailored training allows to generalize the method to the presence of multiple timescales.
4. The method is extendable to experimental data. These findings open new avenues to provide heuristic models for real neurons by stimulating them in closed-loop experiments using, for instance, dynamic-clamp. Unfortunately, we lose any biophysical meaning of the model.

ACKNOWLEDGEMENTS & REFERENCES

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