# Dynamic Reversal Potential Model Reproduces Evolution of Action Potential Attributes

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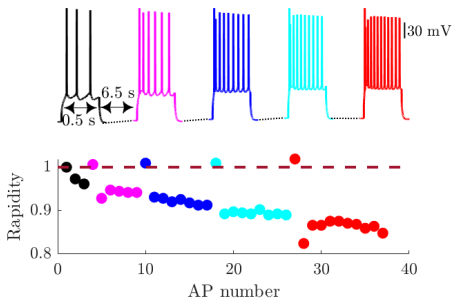
***Abstract* —The shape of neuronal action potentials (APs) evolves during repeated bursts evoked by injected current pulses. The shape of the APs can be quantified in terms of AP width, height, threshold potential, and onset rapidity. Analysis of multistep electrophysiological recordings show mammalian cortical and hippocampal neurons exhibit nearly monotonic variation in these four attributes during stimulation pulses. A large variety of existing neuron models predicted no variation in the AP attributes. However, incorporation of ion concentration dynamics – and thus dynamic reversal potential – reproduced the AP attribute trends and correctly predicted the magnitude of changes for some, including rapidity.**

## I. Analysis of Experimental Recordings

Differences in the shape of action potentials (APs) from various types of neurons and even more so the temporal variation of AP shape provide a window into biophysical mechanisms in neurons. For example, the abruptness of the onset of APs, which we term rapidity, has been used to argue for cooperative interaction between $Na^+$ channels [1], subsequently engendering debate between researchers offering alternative mechanisms [2]. Four shape attributes – width, height, threshold potential, and rapidity – were extracted for every AP in electrophysiological recordings for 51 neurons of three different types from public databases. An example of the normalized rapidity of 37 APs from a regular-spiking cortical neuron in response to 5 pulses of increasing current (40 pA steps) is shown below. Rapidity was analyzed using a method based on the width of the peak of the second derivative of membrane potential [3] allowing rapidity to be used for the first time to classify neuron type [4].




## II. Modeling

Several existing single-compartment models that did not incorporate time-varying ion concentration were investigated, but all failed to reproduce the trends in AP attributes during pulses or from pulse to pulse, instead predicting that the attributes did not vary. However, a new neuron model incorporating transport and buffering, and thus temporal variation, of $Na^+$ and $K^+$ concentrations generates trends in AP attributes that mostly match the experimental observations. These models were previously investigated almost exclusively for pathological conditions [5], but here we investigated healthy neurons. The new model indicates that during stimulation pulses, the $K^+$ concentration almost completely recovers between pulses. However, both the intracellular and extracellular $Na^+$ concentrations move closer to each other with each AP, decreasing the $Na^+$ Nernst or reversal potential during the pulse. Dynamical reversal potential contrasts with the standard assumption in neuron models that reversal potential is a fixed constant for each ion due to large ion reservoirs. We hypothesize that the difference in local ion concentrations proximate to ion channels, and especially ion channel clusters that may play a role in cooperative gating, is significantly depleted during APs and is subsequently replenished from reservoirs by diffusion during times between APs.

## III. Conclusion

A model that includes dynamic reversal potential predicts evolution of AP attributes that much better match experimental data from normal neurons than traditional models that neglect ion concentration dynamics.

## References

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