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**Recovery of Voltage-Gated $Na_v1.4$ Channels from Slow Inactivation Reflects Memory of Prior Stimulation in Multiple Molecular Processes**

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Slow inactivation (SI) regulates availability of voltage-gated $Na^+$ ($Na_v$) channels in neurons, cardiac myocytes and skeletal muscle cells thereby determining excitability. In native cells, inactive $Na_v$ channels accumulate when the time between action potentials is inadequate to allow recovery from SI. SI can be simulated with cloned channels by repetitive application of seconds-long depolarizing pulses to cells expressing the channels. Others have shown that, in contrast to voltage-gated $K^+$ channels, the rate of recovery from SI for $Na_v1.2$ channels (a neuronal isoform) depends on the duration of the previous depolarizing pulse - the channels show memory (Toib et al. 1998. J. Neurosci. 18:1893-903). To investigate this phenomenon in $Na_v1.4$ channels (a muscle isoform), we measure ionic and gating currents in cut-open oocyte mode and employ voltage clamp fluorimetry to correlate motion of each of the four S4 voltage sensing domains with currents. Like $Na_v1.2$, $Na_v1.4$ recovery from SI is found to depend on prepulse duration. A model for memory of prepulse duration is proposed based on the kinetics of processes associated with specific S4 domains and others independent of gating charge movement.