

# Encoding of Constant Temperatures and Temperature Changes: A Comprehensive Model of Temperature Transduction.

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Cold sensitive skin receptors are characterized by spontaneous discharges at constant temperatures with dynamic frequency overshoots on fast cooling and transient inhibition on fast warming. The frequency overshoot of mammalian cold receptors was recently ascribed to transient currents through cold and menthol sensitive ion channels (TRPM8) while the same response characteristic in cold sensitive shark electroreceptors was related to temperature induced gel currents (e.g. Reid and Flonta, *Nature* 413, 480, 2001; Brown, *Nature* 421, 495, 2003). However, these findings do not consider static impulse generation at constant temperatures and the particular temporal structure of the discharges which was attributed to systematic modulation of noisy subthreshold oscillations (e.g. Braun et al., *Nature* 367, 270, 1994) and recently could be simulated in a Hodgkin-Huxley type computer model with temperature dependent changes of time constant of ion channel activation (e.g. Braun et al., *Biosystems* 71: 39-50, 2003).

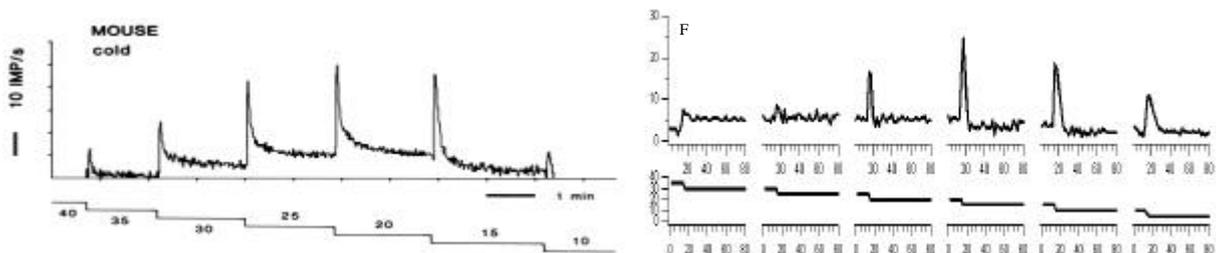


Fig. 1: Experimentally recorded firing rates of a mouse cold receptor during successive cooling steps (left) and corresponding data from computer simulations (right).

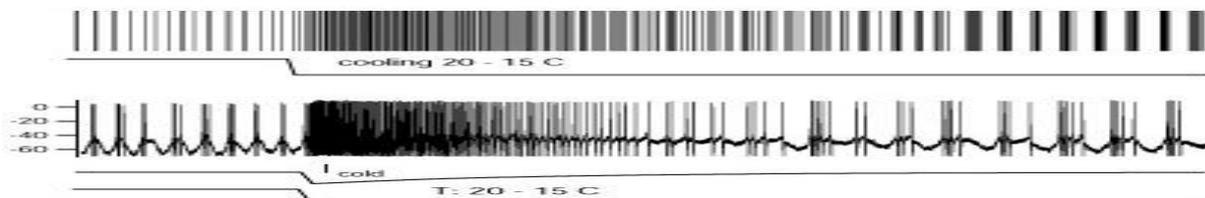


Fig. 2: Impulse sequence of an extracellular recording from a single peripheral cold afferent (upper trace, action potentials plotted as vertical lines of normalized height.) and corresponding computer simulation (which also shows the spike-triggering membrane oscillations).

We have extended these simulation approaches to develop a comprehensive model which can simulate both static and dynamic responses. Indeed, on the basis of subthreshold, spike-generating oscillations, the principle characteristics can be mimicked with a combination of temperature dependent scaling of time constants (see Braun et al., *Biosystems* 71: 39-50, 2003) and addition of a "cold current" which - irrespective of its particular origin - activates as a function of the slope of a temperature change ( $dI/dT = 1\mu A/cm^2 \cdot s$  per  $^{\circ}C/s$  with a relaxation time constant of 4 s). Fig 1 compares the experimentally recorded frequency-temperature curves of a cold receptor during successive cooling steps (left, data from Schäfer et al. *Pflügers Arch* 412: 188-194, 1988) with the corresponding simulation results (right) both showing the characteristic maximum curves of static and dynamic responses. Fig. 2 demonstrates that also the typical changes of the impulse pattern can be simulated remarkably well. As an example, at mid-temperatures both the real and simulated cold receptor exhibit static burst discharges which are transiently interrupted by high frequent tonic-firing in response to the fast temperature change.

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