# TEMPERATURE EFFECTS ON SIMULATED HUMAN INTERNODAL ACTION POTENTIALS AND THEIR DEFINING CURRENT KINETICS

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## ABSTRACT

**PURPOSE: Action potentials reflect membrane properties in body excitable structures. To expand our studies on these membrane properties, the effects of temperature on internodal (paranodal, mid-internodal) action potentials and their defining current kinetics are investigated.**

**MATERIAL AND METHODS: The computations use our temperature dependent multi–layered model of human motor fibre and the temperature is increased in the range of 20-40°C.**

**RESULTS: For all temperature dependent cases: (i) nodal, paranodal and mid-internodal action potentials are similar, with a small drop to minimal amplitude in the centre of the internode; (ii) transaxonal and transmyelin currents rapidly diminish in amplitude as the distance from the node increases reaching equal minimal values in the intermodal centre; (iii) the current kinetics of the paranodal and mid-internodal action potentials is slightly changed in the physiological range of 32-37°C, and (iv) internodal ionic currents beneath the myelin sheath ($I_{Na}$, $I_{Kf}$, $I_{Ks}$, $I_{IR}$, and $I_{Lk}$) are not temperature-dependent.**

**CONCLUSION: The effects of temperature on the paranodal and mid-internodal action potentials are the same as those on the nodal action potentials. However, the temperature effects on their current kinetics are quite different, because ion channels under the myelin are insensitive to the temperatures and short current impulses used in this study. The results obtained are important for the interpretation of temperature dependent nerve conduction measurements in health.**

**Key words:** *temperature, action potential, current kinetics, human motor nerve axon, computational neuroscience*

## INTRODUCTION

The passive (resistance, capacitance) and active (ion channel) properties of the nodal, paranodal and intermodal segments form a quantitative description of the action potential propagation in these segments along the fibre length. This allows one to determine, for example, the sensitivity of intermodal action potentials to the temperature changes. The effects of temperature on standard measures of nerve conduction are well established. The nerve conduction velocity increases by ~5% per degree C as the temperature increases from 29 to 38°C (3,4,6), whereas the nerve amplitude slightly decreases (1,2,5). The temperature effects have longer been simulated on nodal action potentials in myelinated fibres. However, the temperature effects on the intermodal action potentials have not been studied yet.

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The aim of this study is to investigate and show the changes of intermodal (paranodal, mid-internodal) action potentials in human motor nerve fibres and to provide a deeper understanding of the mechanisms underlying these changes when the temperature increases from 20 to 40°C.

## MATERIAL AND METHODS

The simulations presented here apply our modified temperature dependent model of motor nerve axons (8). It is derived from our previous multi-layered model of human motor nerve fibre (7,9) in which the myelin sheath aqueous layers provide appreciable longitudinal and radial conductance. In the modified and normal multi-layered model, the myelin sheath is presented as a series of 150 interconnecting parallel lamellae. The model axon comprises 30 nodes and 29 internodes. Each internode is divided into two paranodal and five intermodal segments. The lengths of node, paranode and nodal centre to nodal centre are 1,5; 200 and 1400 μm. All calculations are carried out for fibres with an axon diameter of 12,5 μm and an external fibre diameter of 17,3 μm. The temperature dependent intermodal (paranodal and mid-internodal) action potentials and their defining current kinetics are investigated in the range of 20-40°C. The action potential stimulation is simulated by adding a short (0,1 ms) rectangular depolarizing current pulse to the centre of the first node.

## RESULTS

Our model permits to distinguish between the intranodal and extranodal potentials along the fibre length. Fig. 1 shows action potentials at node 10, adjacent distal paranode and mid-internode between nodes 10 and 11 at temperatures given in the panel figures. To provide a better illustration, x-scales of the panel figures are different in the first and second columns. For all investigated temperature-dependent cases, the nodal, paranodal and mid-internodal action potentials are similar, with a small drop to minimum amplitude in the centre of the internode. Maximal amplitudes for the three types of action potentials increase up to 37°C and then decrease, along with the increase of temperature from 20 to 40°C. The potential amplitudes are slightly changed in the physiological range of 30-37°C. The potential duration progressively decreases with the progressive increase of the temperature. For all investigated temperatures, the conduction velocities calculated from the times of the potential maxima at the paranodes or at the mid-internodes are equal to those calculated from the times of the potential maxima at the nodes.

The temperature dependent paranodal and mid-internodal action potentials as nodal action potentials are determined by their current kinetics (Fig. 2 and Fig. 3). Using our model, we can also distinguish between the transaxonal current across the internodal axolemma ($I_a$, Fig. 2 and Fig. 3) and the transmembrane current ($I_m$, Fig. 2 and Fig. 3) across the myelin sheath. In the mid-internodal segments, the external membrane current ($I_m$, Fig. 2b and Fig. 3b) is equal to the transmyelin current. For all investigated temperatures, the transaxonal and transmyelin currents rapidly diminish in amplitude as the distance from the node increases, reaching equal minimal values in the centre of the internode ($I_a$, $I_m$, Fig. 2b and Fig. 3b). Increased amplitude of the transmembrane currents in the paranodal segments is realized when the temperature increases ($I_m$, Fig. 2a and Fig. 3a). However, considerably more outward current flows across the paranodal axolemma ($I_a$, Fig. 2a and Fig. 3a) than it is apparent from the current flowing across the membrane ($I_m$, Fig. 2a and Fig. 3a).

The current kinetics of the paranodal and mid-internodal action potentials is slightly changed in the physiological range of 32-37°C (Fig. 3). For all investigated temperatures, the internodal ionic currents beneath the myelin sheath ($I_{Na}$, $I_{Kf}$, $I_{Ks}$, $I_{IR}$, and $I_{Lk}$) are not significantly changed during the action potentials either at the paranode and mid-internode and appeared as straight lines at Fig. 2 and Fig. 3, respectively.

## DISCUSSION

In this paper we determined the temperature effects on the intermodal action potentials of human motor nerve fibres. The most essential and significant result is that the effects of temperature on the paranodal and mid-internodal action potentials are similar to those on the nodal action potentials. However, the temperature effects on their current kinetics are quite different, because the ion channels under the myelin are insensitive to the temperatures

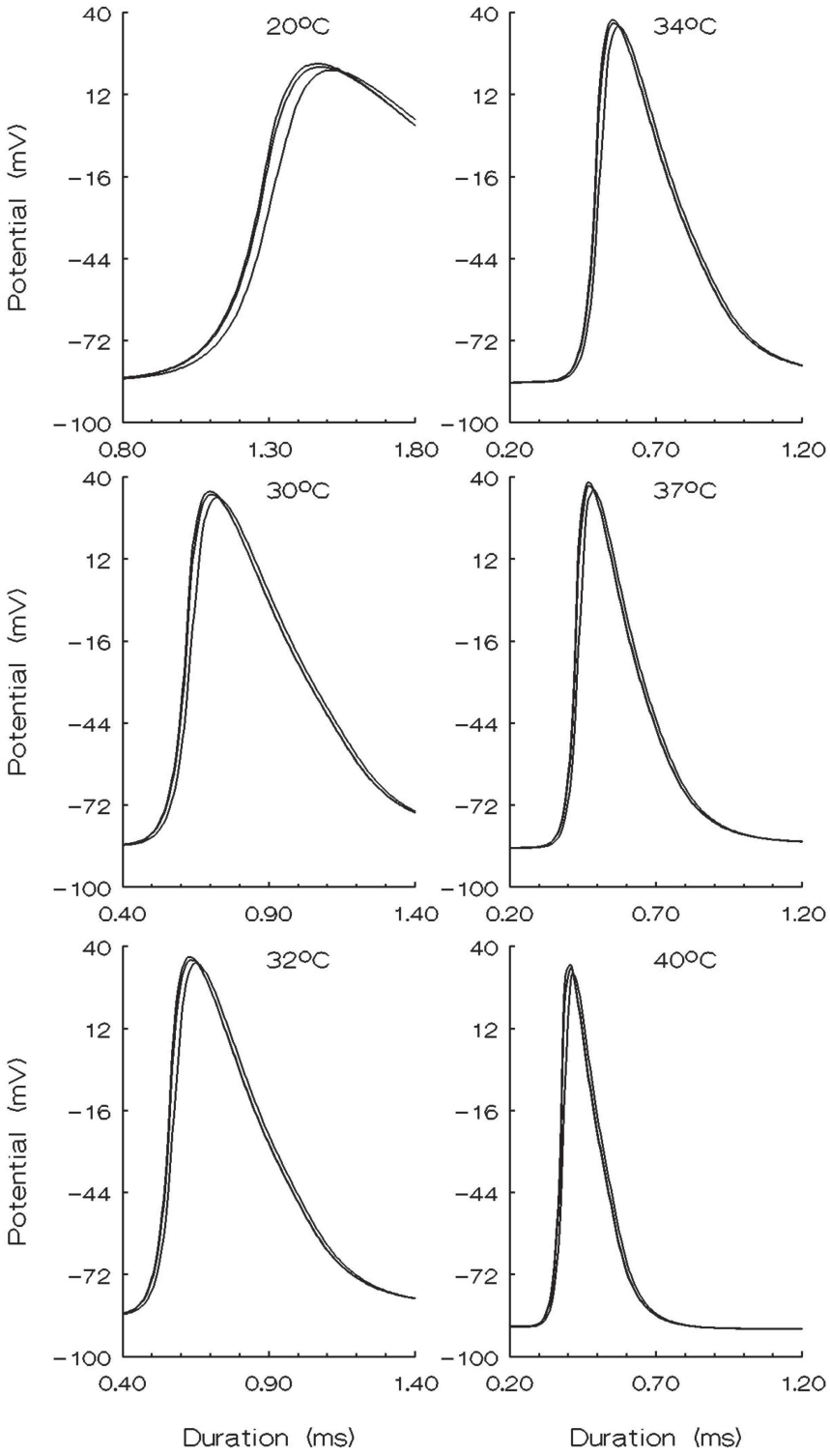


*Fig. 1. Action potentials of human motor nerve fibre at node 10, adjacent distal paranode and mid-internode between nodes 10 and 11 at temperatures given in the panel figures. Note that the x-scales of the panel figures are different in both columns*



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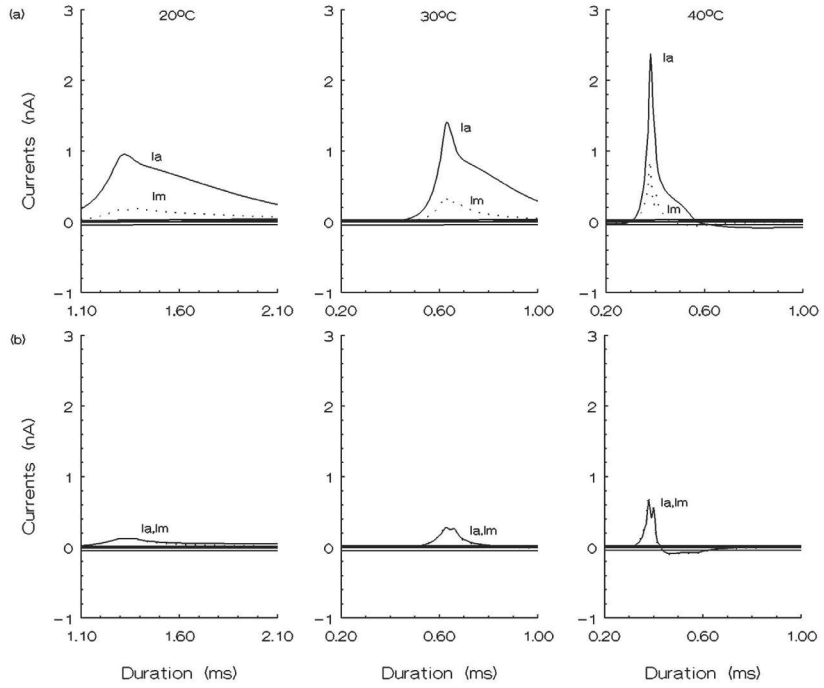


*Fig. 2. Current kinetics defining the action potentials at paranode next to node 10 (a) and mid-internode between nodes 10 and 11 (b) at temperatures given in the panel figures. Currents: $I_a$ (transaxonal), $I_m$ (external membrane, dotted lines), $I_{Na}$ (sodium), $I_{Kf}$, $I_{Ks}$ (fast, slow) potassium, $I_{IR}$ (inward rectifier), $I_{LK}$ (leak). In the mid-intermodal segments, the external membrane current is equal to the transmyelin one. Straight lines indicate the intermodal ionic currents $I_{Na}$, $I_{Kf}$, $I_{Ks}$, $I_{IR}$, and $I_{LK}$, respectively*

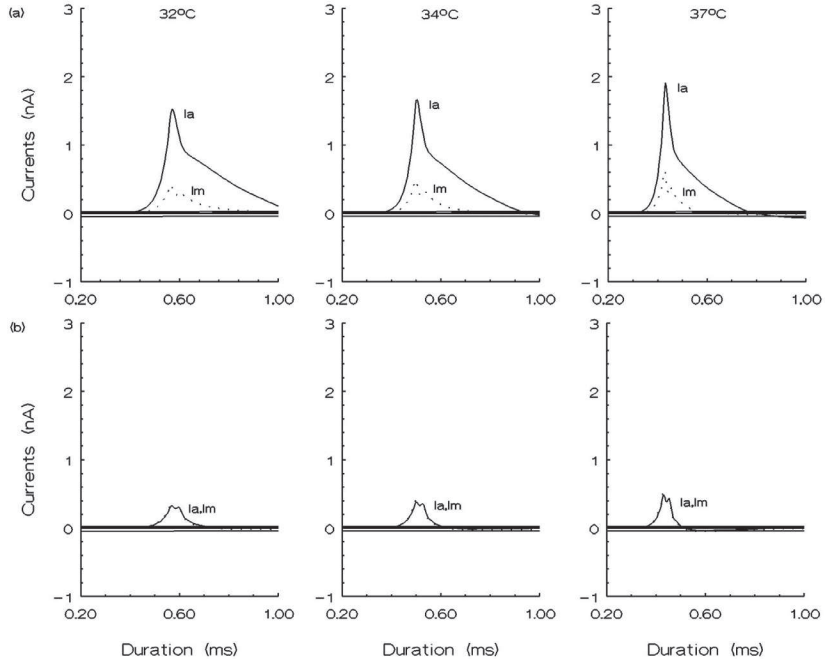


*Fig. 3. Current kinetics defining the action potentials at paranode next to node 10 (a) and mid-internode between nodes 10 and 11 (b) at temperatures given in the panel figures. Currents: $I_a$ (transaxonal), $I_m$ (external membrane, dotted lines), $I_{Na}$ (sodium), $I_{Kf}$, $I_{Ks}$ (fast, slow) potassium, $I_{IR}$ (inward rectifier), $I_{LK}$ (leak). In the mid-intermodal segments, the external membrane current is equal to the transmyelin one. Straight lines indicate the intermodal ionic currents $I_{Na}$, $I_{Kf}$, $I_{Ks}$, $I_{IR}$, and $I_{LK}$, respectively*

and short current impulses used in this study. Our results are reported for the first time. They are important for the interpretation of temperature dependent nerve conduction measurements in health.

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