Impact of Electrode Position on the Dynamic Range of a Human Auditory Nerve Fiber

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Research Article

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Impact of electrode position on the dynamic range of a human auditory nerve fiber

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Electrodes of a cochlear implant generate spikes in auditory nerve fibers. While the insertion depth of each of the electrodes is linked to a frequency section of the acoustic signal, the amplitude of the stimulating pulses controls the loudness of the related frequency band. The firing efficiency of an auditory nerve fiber, stimulated by a train of pulses varies between 0 and 100\%. 100\% firing efficiency means every pulse elicits a spike, 50\% defines threshold. The dynamic range of an auditory nerve fiber is the range of stimulus intensities that causes a firing probability between 10 and 90\%. This ‘electrical’ dynamic range is quite small in comparison to the variation of spiking rates measured during acoustic stimulation. Consequently, an increased dynamic range may improve the quality of auditory perception for cochlear implant users. Electrodes are often placed as close as possible to the center axis of the cochlea. Analysis of simulated auditory nerve firing showed that this placement is disadvantageous for the dynamic range. Five times larger dynamic ranges are expected for electrodes close to the terminal of the dendrite or at mid-dendritic placement.

The cochlea operates as a frequency analyzer where every inner hair cell mimics a band pass filtered microphone by transforming a small frequency band of the acoustical signal into an analog intracellular voltage. A single synaptic connection between an inner hair cell and the distal end of an auditory nerve fiber (ANF) converts this analog signal into a digital signal as a train of action potentials (spikes). According to this principle the spiking rate (spikes/s) of any afferent auditory nerve fiber increases with the loudness of the corresponding frequency.

The physiological task of the main part of the auditory nerve is a data bus that transfers all the action potentials (AP) generated by inner hair cells to the next neural processing center, the cochlear nucleus. In more anatomical detail, each element of the data bus is a so called type-I spiral ganglion cell consisting of a dendrite, a soma, and an axon, where the diameters and the degree of myelination changes along the cell axis. These details have less impact for synaptic stimulation in the healthy ear in comparison with electrical stimulation where (i) spike initiation site depends on electrode position, (ii) thin degenerated dendrites may not be excited, and (iii) polarity sensitivity depends on cochlear status\textsuperscript{1-4}.

When generated from a cochlear implant (CI), the spiking patterns of the auditory nerve show severe deficits versus natural hearing\textsuperscript{5-8}. Especially for difficult neural decoding tasks such as speech understanding in noisy environment, every single ANF crucially contributes with the own spiking rate and its temporal changes following the loudness variations in the corresponding frequency region of the acoustic source signal.

Spiking probability as a function of stimulus intensity is the key-control element in the input-output relation in functional electrical nerve stimulation. The range of intensities where the spiking probability of an ANF increases from 10\% to 90\% is defined as its dynamic range and indicates a fiber’s individual loudness contribution during CI stimulation\textsuperscript{1}. The firing probability, also called firing efficiency, can be found experimentally as the ratio (number of spikes)/(number of stimulating pulses). In the schematic diagram of Fig. 1 the spiking probability was extracted from five series á 100 pulses marked by x. The threshold (700 µA) is defined by the 50\% firing efficiency and the dynamic range was 128 µA which is 18\% (128/700). Note that the dynamic range during acoustic stimulation\textsuperscript{5,8} is about two orders
larger in comparison with this example that is typical for electrical stimulation of feline ANFs\textsuperscript{9}.

Verveen\textsuperscript{10} introduced relative spread (RS) as another measure for the stochastic nature of an electrically stimulated nerve fiber. He plotted the firing probability in a similar way as shown by markers (x) in Fig. 1 and noted that the counted spike numbers approximated that of an integrated Gaussian curve. RS is the standard deviation of that Gaussian function divided by threshold. Comparison of both measures shows that the dynamic range (normalized by threshold) is 2.56 times RS.

From peripheral nerve fiber stimulation experiments Verveen estimated log RS = -1.5 - 0.8*log d (diameter d in µm), which specifies how RS decreases with diameter\textsuperscript{11}. Our RS example of Fig. 1 for 1µm diameter ANF fibers is more than twice the 3\% (0.03) of Verveen’s formula but it is still not comparable to acoustic stimulation where an increase from 25 to 150 spikes per second results from a stimulus (= loudness) increase of about 1000\%\textsuperscript{8}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Relationship between stimulus intensity, firing efficiency, dynamic range, and relative spread. An integrated Gaussian curve is used to fit the counted spike numbers marked by x. The slope of this firing efficiency curve at threshold can be used for a guess of the dynamic range. The spread (magenta) is related with the dynamic range (cyan) by the formula (normalized) dynamic range = 2.56 x RS.}
\end{figure}

Based on an electrical circuit model with ion current fluctuations across the cell membrane, the actual study estimates the impact of electrode position on the dynamic range for human standard ANFs and ANFs with degenerated diameters. Following an approach of Rattay\textsuperscript{12}, a noise current is added in every segment with an active membrane (nodes of Ranvier, non-myelinated terminal, somatic region). Each segment’s simulated noise current is proportional to the square root of the number of its sodium channels\textsuperscript{12,13}.

In this modeling study we show that the dynamic range increases with the electrode distance to the central axis of the cochlea.
Results

Dynamic range of a feline ANF. In our simple model approach a single parameter knoise for Gaussian N(0,1) controls all stochastic effects. In a proof of concept knoise was set to 0.00125 (with unit µA mS\(^{-1/2}\), see method section for details). The ANF consisted of a dendrite (diameter d1=1 µm), 3 node – internode combinations with an internode length of 150 µm\(^{14}\), a myelinated spherical soma (d=15 µm, covered with 13 sheets of membrane)\(^{15}\) and a 4 mm long axon (d2=2 µm, internode length = 300 µm). The electrode center was 300 µm above the center of the dendrite and the axis of the cell was a straight line (Fig. 2). For a period of 0.5 ms before stimulus onset the enlarged plot of membrane voltage accurately demonstrated the decrease of membrane voltage fluctuations with increase of diameter as predicted by theory (Fig. 2, bottom). In this example where \(d2 = 2 \times d1\), the surface of the axonal node is twice the dendrite node but its noise current increases only by a factor \(\sqrt{2}\). Indeed, the Vm range decreased from 2.4 to 1.7 which is exact the theoretical ratio \(\sqrt{2}/1\).

Figure 2. Simulated response of a feline ANF to cathodic and anodic 100 µs pulses. The transmembrane voltage Vm of every compartment is shown as a single line, shifted vertically according to the compartment number: nodes of Ranvier (green, peripheral nodes P and central nodes C), internodes (blue), soma (black). For cathodic stimulation, the strongest responses are expected in the nodes of Ranvier closest to the electrode. These are peripheral nodes P1 and P2. At pulse onset the slope of Vm in the active compartments changes along the ANF three times the sign of direction, indicating whether the stimulus has a positive (polarizing) or negative (hyperpolarizing) impact. The sequence of signs -(terminal), +(P1), +(P2), +(P3), +(C1), -(C2), -(C3), -(C4) favors P2 to be the site of spike initiation. During the anodic pulse the whole dendrite is hyperpolarized and the spike is elicited in the second axonal node C2. Enlarged Vm signals (bottom) demonstrate smaller oscillations in the thicker axon.
Application of cathodic 100 µs pulses resulted in a threshold current of 99.7 µA, RS = 5.05% and a dynamic range of 12.86 µA (12.9% normalized to threshold). This RS is between Verveens 3% and data of Miller and coworkers\(^9\) where RS values between 2 and 20% (mean 6.6%) based on single ANF recordings were reported. Consequently, we used the same knoise=0.00125 for the human case where no single fiber recordings are possible because of ethical reasons.

Changing just the polarity and applying a positive pulse needs about doubled electrode current to elicit an AP which is initiated in the axon as both the complete dendrite and the soma is hyperpolarized during pulse application (Fig. 2). In comparison to cathodic stimulation RS is reduced from about 5% to 3%, which is a consequence of spike initiation in the thicker axon.

**Dynamic range for electrode positions close to an ANF in a human cochlea.** CIs are commonly inserted at the round window into scala tympani, the lower cavity of the cochlea. The electrodes are positioned either close to the outer wall or central close to the modiolus but also they may be placed in between (Fig. 3). In comparison with the feline ANF, in human the dendrite is longer and a bit thicker, there is a non-myelinated pre-somatic region, the soma is larger and non-myelinated, the axon is thicker and longer (Table 1).

![Figure 3](image.png)

**Figure 3.** Main part of a midmodiolar cross-section of a human cochlea with 2 target ANFs in the basal and middle turn and possible electrode placements for an electrode center distance of 300 µm to the ANF. The ANF has a two-dimensional curved pathway consisting of a 1.1 mm long dendrite with 4 nodes of Ranvier, a non-myelinated soma region and a myelinated axon.

In contrast to the straight cell axis of the feline example a curved two-dimensional ANF as introduced by earlier work\(^2\) (Fig. 3) was evaluated to study more realistic electrode distances. Threshold and RS were calculated for four electrode positions, again with a constant distance of 300 µm between electrode center and ANF axis: at the terminal, the dendrite center, close to the soma and 200 µm further in central direction. The last position is not possible in most human cochlea turns but it is of interest for demonstrating the threshold sensitivity of the axon versus the dendrite.
length [µm] | diameter [µm] | source
---|---|---
terminal | 10 | 1.35 | 12

dendrite | 1100 | 1.35 | 15

dendritic internode | 200 *) | 1.35 | 2

presomatic compartment | 100 *) | 1.35 | 2

spherical soma | 20 | 20 | 15

axon | 4000 | 2.67 | 15

axonal internode | 400 *) | 2.67 | 2

node of Ranvier | 1.5 | 1.35 or 2.67 | 2

**Table 1.** Morphometric parameters for a healthy human ANF. For myelinated compartments the inner (axon) diameter is listed. In reality the non-myelinated terminal is longer and thinner but in the model it is substituted by a compartment with dendrite diameter d1 and a surface close to the real one. The total human ANF length is about 32mm but for this study the axon was cut at 4mm to reduce computational costs.

*) no data available from literature

Dendrite diameters are often reduced in persons with hearing deficits. A recent study reported a peak in the dendritic (inner) diameter histogram at d1 = 0.5 µm and diameters down to 0.3 µm recorded from a profound deaf ear. Table 2 shows the threshold and RS values for monophasic 100 µs pulses for a normal ANF with parameters of Table 1 and the corresponding data when just the dendrite diameter is reduced to half of the standard value. As expected, RS increases for all positions and both polarities if the diameter is reduced (Table 2, degenerated ANF).

| electrode position at | healthy ANF d1=1.35 [µm] | degenerated ANF, d1=0.7 µm |
|---|---|---|
| | cathodic pulse | anodic pulse | cathodic pulse | anodic pulse |
| | threshold [µA] | RS [%] | Threshold [µA] | RS [%] | threshold [µA] | RS [%] | threshold [µA] | RS [%] |
| terminal | -114.7 | 9.58 | +225.0 | 2.50 | -176.7 | 15.83 | +244.9 | 4.49 |
| mid dendrite | -115.9 | 4.15 | +105.9 | 8.76 | -138.6 | 6.12 | +124.6 | 15.22 |
| soma | -470.1 | 2.31 | +119.8 | 1.74 | -529.0 | 3.20 | +119.8 | 1.85 |
| axon 200 µm after soma | -77.1 | 1.05 | +82.4 | 1.05 | -77.2 | 1.07 | +82.4 | 1.07 |

**Table 2.** Thresholds and RS values for a healthy ANF and for a reduced dendrite diameter. Stimulation with monophasic cathodic and anodic 100µs pulses.

For cathodic pulses RS is largest for the terminal electrode and the values decrease with the electrode distance from the terminal. For anodic stimulation the excitation process is more complicated and spike initiation site is commonly further away from the electrode. The mid-dendritic electrode has the largest RS for an anodic pulse, followed by a quite smaller RS for the terminal position. The large anodic RS for the mid-dendritic position is related with the more complicated excitation process which enable anodic pulses to initiate spikes both in the dendrite and in the axon, see Fig. 4.
The characteristic dependence of dynamic range (about 2.56 times RS) on diameter \(d_1\), electrode position and polarity is also shown in Fig. 5. According to the reversed recruitment order thicker fibers have lower thresholds\(^{18,19}\) which favors spikes to be elicited in the axon. On the other hand, an electrode can be placed closer to the dendrite resulting in a competition between dendrite and axon for the site of spike initiation. Accordingly, the low threshold value for the last electrode position in Table 2 is essentially lower than at the dendrite. As mentioned before, the shape of the scala tympani may hinder in many cases to set an electrode very close to an ANF axon (compare Fig. 2).

![Figure 4. Latencies of spikes until they arrive at central node C4 depend on spike initiation site and stimulus intensity. Cathodic stimulation causes spike initiation always in the dendrite (a, b), whereas spikes generated by anodic pulses can be elicited in the dendrite (c, weak stimulation) or both in dendrite and axon (d, stronger stimulation). In case e two spikes are generated, one in dendrite one in the axon; however, when the dendritic spike arrives at the axon it is stopped by collision and generates a weak (subthreshold) second excitation. The large jitter at threshold (a, c) is tremendously reduced already at 1.2 times threshold (b, e). The green rectangle indicates a 240 µs longer delay for spikes generated in the dendrite. 10 runs per case, electrode in mid-dendritic position, \(d_1=1.35 \, \mu m\).

The ratio of axon diameter \(d_2\) and dendrite diameter \(d_1\) has a large impact on the decision whether the spike is generated in the dendrite or in the axon. While for \(d_1 > 0.6 \, \mu m\) the terminal electrode position preferentially initiates dendritic spikes, a change to the axon is shown in Fig. 5.
Figure 5. Spiking efficiency with color coded spike initiation site for an electrode at the terminal (a-c), at mid-dendrite (d-e), and soma position (f). Cathodic stimulation: Even for a thin dendrite of diameter d1=0.7 µm almost all spikes are initiated in the dendrite (a) but reduction to d1 = 0.6 µm favors spike generation in the axon, especially for stronger pulses. Further reduction of d1 to 0.5 µm initiate most spikes in the axon (c). A shift of the electrode from terminal to mid-dendrite position increases axonal spike initiation (a vs. d). Note the decreased dynamic range (marked as green lines) for mid-dendritic (d) versus terminal (a) electrode position and the increase of dynamic range for reducing diameter (a-c). For anodic stimulation dynamic range of mid-dendritic electrode position is larger than the cathodic (e vs. d) and for anodic soma position (e vs. f). Stimulation with 100µs pulses, 500 pulses for each bin, intensities relative to threshold.

In the next example, spike initiation site for stimulation with biphasic pulses, 50 µs per phase, are studied for the mid-dendritic electrode position. Two cases are compared concerning the polarity of the first phase. Cathodic first stimulation needs less current versus anodic first and for both polarities spikes are elicited in the terminal P0 by the anodic phase (Fig. 6). Surprisingly, the anodic phase is in this case more effective. However, it is a combination of the ANF pathway relative to the electrode position and the 2 phases which lets P0 win the threshold competition. Several other compartments, marked by dashed lines in Fig. 6, are
candidates for the spike initiation site as they are close to threshold voltage during the stimulation period. A small increase of the electrode current would make one of them the winner during the first phase. For cathodic first stimulation, P1 reached the highest membrane voltage \( V_m \) in the first phase, followed by P2 and P4. The inset on the top of Fig. 6 shows \( V_m \) of P0 and P1 at the same baseline (without the vertical shift for each compartment) and demonstrates that \( V_m \) at P1 (dashed green line) essentially exceeds \( V_m \) at P0 during the stimulation time. A small variation of the noise signal can initiate the spike in P1. Note that the second phase was able to stop spike excitation in P1, but for comparison a quite similar condition enables to generate the P0 spike in the anodic first phase (Fig. 6b) in spite of the repolarizing second phase. For the anodic first pulse the axon compartment C2 is the second candidate for the spike initiation site.

Thresholds and RS are listed in Table 3 for both polarities of biphasic pulses. All electrode positions with exception of soma have lower thresholds for cathodic first pulses. In comparison with Table 2, the thresholds (again with exception of soma) are essentially higher for the short 50 \( \mu \)s phase. In contrast to monophasic pulses the RS differences are similar for terminal and mid-dendritic position. For the biphasic case, terminal and mid-dendritic position has more than five times higher RS values as at the axon.

| electrode position at | +- threshold [\( \mu A \)] | RS [%] | -+ threshold [\( \mu A \)] | RS [%] |
|----------------------|-----------------------------|--------|-----------------------------|--------|
| terminal             | 419.9                       | 5.82   | 368.5                       | 6.85   |
| mid dendrite         | 231.9                       | 5.57   | 193.4                       | 5.61   |
| soma                 | 345.1                       | 1.12   | 517.8                       | 1.17   |
| axon 200 \( \mu m \) after soma | 168.9               | 1.02   | 165.3                       | 1.02   |

**Table 3.** Thresholds and RS for biphasic stimulation, 50 \( \mu s \) per phase. +- means anodic pulse first and vice versa.

**Discussion**

The resolution of loudness perception of each of the frequency bands covered by the electrode array of a CI is a bottle neck for electrical stimulation. The dynamic range of an electrically stimulated ANF is at least one order lower than its dynamic range during acoustic input. Thus, in comparison to natural hearing, neural patterns generated from CIs miss a lot of acoustic information. According to the presented modelling study electrode placement has a large impact on the dynamic range of a target ANF. A good electrode place for a larger dynamic range is close to the dendrite but without being close to the soma or axon.

The model predicts a surprisingly large polarity dependence of the RS ratio for the electrode positions terminal and mid-dendrite. According to Table 2 cathodic pulses cause 2.3 times larger RS for terminal vs. mid-dendrite, whereas for anodic pulses mid-dendrite has the largest RS with a ratio of 3.5 for these positions. Halving of dendrite diameter, a consequence of degeneration related with hearing deficits\(^4\), showed a RS increase close to the theoretical value of \( \sqrt{2} \) and caused quite similar RS ratios for terminal and mid-dendrite.

This extreme polarity dependence of monophasic pulses seen for terminal and mid-dendritic electrode positions is changed in direction of average values for biphasic stimulations (Tables 2 and 3) with rather small differences with respect to the leading pulse polarity.
Figure 6. Spike initiation with biphasic pulses about 10% above threshold, 50 µs per phase, from an electrode in mid-dendritic position. Spike initiation is here always in the terminal P0 during the anodic phase. Several other compartments, marked by dashed lines, are candidates for spike initiation sites if stimulus intensity is increased. Insert at top of a) contrasts size of membrane voltage Vm at P0 against P1 during pulse application, demonstrating a high Vm of P1 at the end of the first pulse which fails to generate a spike in the way as it was possible by the magenta Vm curve of P0 in b).

Biphasic pulses are commonly used in CIs. For such pulses, model evaluations predict for both terminal and mid-dendritic positions a five times larger dynamic range compared to electrodes close to the soma or to the axon (Table 3). This advantage of a large dynamic range depends, however, on the degeneration status of the dendrite. Degeneration of an ANF means either the loss of its dendrite or a reduction in diameter\(^4,20,21\). In cochlear regions where the greater part of ANFs lost their whole dendrites it is not advantageous to place the electrode close to the outer wall.
Limitations of the model. The purpose of the study was a first approach of the dynamic range of human ANFs and its dependence on electrode positions in the scala tympani. A more accurate model should be based on the geometry and the tissue depending electrical conductances of the human cochlea as well as on morphometric details of ANFs including their 3-dimensional pathways\textsuperscript{4,22-27}. Considering more details enables better predictions, e.g. (i) for possible electrode positions close to the axon and the soma which vary with the cochlear turns, (ii) on the effect of reduced myelinization or (iii) on the impact of spatial fine structure of ANFs.

A fundamental problem is the modeling concept for the noisy currents to simulate post-stimulus and interval histograms as observed in electrically stimulated ANFs\textsuperscript{1,6,28,29}. Here, we used a computationally efficient approach (Rattay 2000) which assumes a noise current with constant rms (root mean square) amplitude that reflects the prominent impact of each single sodium channel in the cell membrane (Sigworth 1980). A single parameter, $k_{\text{noise}}$, defines the stochasticity of every compartment via its maximum sodium ion conductance. A more realistic fit incorporates how current fluctuations depend on ion channel gating\textsuperscript{30} or introduces correction terms for fiber diameters and membrane voltage\textsuperscript{31}. In comparison with the last two methods, our approach overestimates the current fluctuations in the resting state. However, the chosen $k_{\text{noise}}$ parameter fit the RS of feline ANFs which are a bit smaller in diameter than the human ones. Reported RS mean values for cat monophasic, monopolar stimulation were 6.6%\textsuperscript{9}, 9%\textsuperscript{1} and Dynes\textsuperscript{32} found RS in the range 5-10%. Our model test for a straight feline ANF ($d_1 = 1 \, \mu m$, $d_2 = 2 \, \mu m$, electrode at mid-dendrite, Fig. 2) resulted in RS of 5 and 3% for cathodic and anodic pulses, respectively. The cathodic 3% RS value is exact in accordance with Verveen’s formula for peripheral axons. Verveen did not observe polarity dependent differences in his data. According to Table 2 ($RS = 1.05$), the human axon diameter of 2.67 $\mu m$ underestimates the RS = 1.81% of Verveen’s formula. Comparing all these RS data, a judgement of our results point to a bit larger $k_{\text{noise}}$ value as our values are comparable with the lower border of the reported RS range. Tests showed a rather linear relationship between $k_{\text{noise}}$ and RS for small changes\textsuperscript{33} which makes it easy to calculate an adjustment factor to be in accordance with reported RS of a specific article. Moreover, RS was reported to be quite independent of pulse duration\textsuperscript{30}.

Methods

A type 1 spiral ganglion cell, which connects an inner hair cells with a neuron in the cochlear nucleus, consists of several subunits as shown in Fig. 7a with parameters listed in Table 1. Every of these subunits, terminal, internode, node of Ranvier, etc. is simulated as a single compartment with exception of four compartments for the non-myelinated presomatic segment. According to Fig. 7a, the cell consists of segments with active membranes with high (marked red) and low ion channel density (pink). Additionally, there are myelinated internodes (gray) where the membrane is assumed to be passive, which means no voltage sensitive ion channel gating mechanisms are considered. The high ion channel density, here modeled as 10 fold Hodgkin Huxley membrane conductance, is needed for signal amplification along the neural pathway\textsuperscript{12,34}. This sodium channel density is comparable to nodes of Ranvier in axons of the mammalian peripheral nerve system\textsuperscript{35,36}. Beside the peripheral terminal and the nodes of Ranvier, the high sodium concentration is applied in the pre- and postsomatic compartment.
Figure 7. Compartment model of a type I spiral ganglion cell. a) Geometry. Myelinated segments are shown in gray. Excitable (active) membranes with high ion channel densities (red segments) in the peripheral terminal P0 and in the nodes of Ranvier are needed for spike amplification. b) Electrical network model. The currents are defined by extracellular potential $V_e$, intracellular potential $V_i$, membrane capacitance $C_m$, membrane conductance $G_m$ and intracellular resistance $R$. A noise current is applied to each compartment with an active cell membrane.

Applying Kirchhoff’s law (the sum of all currents is zero) to the n-th compartment of the electric network of Fig. 7b results in

$$\frac{d(V_{i,n} - V_{e,n})}{dt} C_{m,n} + I_{i,n,n} + \frac{V_{i,n} - V_{i,n-1}}{R_n/2 + R_{n-1}/2} + \frac{V_{i,n} - V_{i,n+1}}{R_n/2 + R_{n+1}/2} = 0 \quad (1)$$

where the first two terms are capacitance current and ion current across the membrane whereas the next two terms describe the intracellular current flow to the left and right compartment. Introducing the reduced membrane voltage $V = V_i - V_e - V_{rest}$ ($V_i$, $V_e$ and $V_{rest}$ are the intracellular, extracellular and resting potential, respectively) leads to the following system of differential equations$^{12,36,37}$

$$\frac{dV_n}{dt} = \left[ -I_{i,n,n} + \frac{V_{n-1} - V_n}{R_{n-1}/2 + R_n/2} + \frac{V_{n+1} - V_n}{R_{n+1}/2 + R_n/2} \right] / C_{m,n}$$

$$\quad + \left[ \frac{V_{e,n-1} - V_{e,n}}{R_{n-1}/2 + R_n/2} + \frac{V_{e,n+1} - V_{e,n}}{R_{n+1}/2 + R_n/2} \right] / C_{m,n} \quad (2)$$

For the first (last) compartment Eqs. 1 and 2 have a reduced form because of lack of neighbors. The membrane surface $A_n$ of every compartment has to be calculated to find $C_{m,n} = A_n C_{m,n}$ ($C_{m,n}$ is the specific membrane capacitance; note that the capacitance of $N$ layers of membranes is proportional to $1/N$). In order to calculate the extracellular potentials $V_e$, needed in Eq. 2, we assumed an infinite homogeneous extracellular medium. Ignoring capacitance effects of tissue, the extracellular potential was calculated as

$$V_e = \rho_e \cdot I_{electrode} / 4\pi r \quad (3)$$

where $r$ is the center-center distance between a compartment of interest and a spherical electrode. $\rho_e = 300$ Ohm.cm was assumed to be the mean resistivity of the extracellular medium$^2$. 

- **Figure 7**. Compartment model of a type I spiral ganglion cell. a) Geometry. Myelinated segments are shown in gray. Excitable (active) membranes with high ion channel densities (red segments) in the peripheral terminal P0 and in the nodes of Ranvier are needed for spike amplification. b) Electrical network model. The currents are defined by extracellular potential $V_e$, intracellular potential $V_i$, membrane capacitance $C_m$, membrane conductance $G_m$ and intracellular resistance $R$. A noise current is applied to each compartment with an active cell membrane.
The ion membrane current is governed by the gating mechanisms of specific voltage sensitive ion channels. It consists of two components

\[ I_{\text{ion}} = A_n \cdot i_{\text{ion},n} + I_{\text{noise},n} \]  

(4)

where \( i_{\text{ion}} \) is the ionic membrane current density and \( I_{\text{noise},n} \) represents ion channel current fluctuations in active compartments. The effective noise current measured in \( \mu A \) is assumed to be proportional to the square root of the number of sodium channels within a compartment

\[ I_{\text{noise},n} = \text{GAUSS} \cdot \text{knoise} \cdot \sqrt{A_n \cdot g_{Na}} \]  

(5)

where GAUSS is a Gaussian noise current term (mean = 0, \( \sigma = 1 \)) that changes its value every 2.5 \( \mu \)s, k\text{noise} = 0.00125 \( \mu A \) mS\(^{-1/2}\) is a factor common to all compartments, \( A_n \) denotes membrane area in cm\(^2\), and \( g_{Na} \) is the maximum sodium conductance. For the regions simulated with 10-fold channel density, \( g_{Na} = 1200 \) mS/cm\(^2\) for the human soma, \( g_{Na} = 0 \) for all myelinated internodes and cat's soma\(^12\).

In compartments with passive membranes (internodes) the term \( I_{\text{ion}} \) of Eqs. 1 and 2 is a current with constant conductance \( I_{\text{ion}} = g_m A_n V_n / N \), where membrane conductance \( g_m \) is 1 mS/cm\(^2\) and the number of insulating layers of cell membranes \( N \) is 40 and 80 for dendrite and axon, respectively\(^2\).

The ion currents of active membranes were simulated with original Hodgkin Huxley kinetics\(^3\) at a temperature of 28.9°C\(^3\). The system of ordinary differential equations was computed in C++ using the backward Euler method with time steps of 2.5 \( \mu \)s.

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F.R. conceived and designed the study. T.T. performed the computational simulations. F.R. analyzed the data. All authors drafted the manuscript, read and approved the final version.

Additional Information
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