# The representation of periodic sounds in simulated sustained chopper units of the ventral cochlear nucleus

Lutz Wiegrebe* and Ray Meddis#

*Dept. Biologie II, Universität München,
Luisenstr. 14, 80333 München, Germany
Phone: +49 89 5902 609
Fax: +49 89 5902 450
Email: lutzw@lmu.de

#Psychology Department, University of Essex
Wivenhoe Park, Colchester, CO4 3SQ, U.K.
Phone: +44 1206 874882
Fax.: +44 1206 873598
Email: rmeddis@essex.ac.uk

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## Appendix 1. computational details.

### *A. Middle-ear filtering*

Two parallel linear band-pass Butterworth filters were used to model the response of the **guinea pig** middle ear. One filter is second order with an upper cut-off of 25kHz and a lower- cut-off of 4kHz. The other filter is second order with upper- and lower-cut-offs of 30kHz and 700Hz. Both have unity gain in the passband. The input to the filter is sound pressure (μPa). The output, *x(t)*, is scaled by a factor of 1.4e-10 so that it reflects measured stapes velocities in $ms^{-1}$.

The **human** middle ear was simulated using four parallel second-order bandpass filters. The gain and cut-off characteristics are given in Table 1. The stapes scalar was 3e-10 m/s/μPa.

| order | gain | lower cut-off | upper cut-off |
|---|---|---|---|
| 2 | -12 | 100 | 1300 |
| 2 | 1.5 | 350 | 6500 |
| 2 | 5 | 1800 | 5200 |
| 2 | -11 | 7500 | 9900 |

**Table 1 Parameters for parallel filters simulating the human middle ear response.**

## B. Mechanical filtering: DRNL filter

The filtering of the BM is modeled with a 'Dual-Resonance-Non-Linear' (DRNL) filter architecture that has been described and evaluated more fully elsewhere (Meddis *et. al.,* 2001; Lopez-Poveda and Meddis, 2001; Sumner *et al*., 2003b). The input is stapes velocity. The DRNL filter consists of two parallel pathways, one linear and the other non-linear, whose outputs are summed to produce an output, *v(t)* representing the velocity of the cochlear partition (m/s).

The *nonlinear* pathway consists of three identical first-order gammatone filters; a compression function followed by three more identical gammatone filters and then by three first-order Butterworth low passes filters. The compression in the non-linear pathway is described by:

$$v[t] = \mathrm{SIGN}(x[t]) \times \mathrm{MIN}(a|x[t]|, b|x[t]|^{v})$$

where *a, b* and *v* are parameters determining the exact behaviour. The compression exponent, *v,* was 0.1 for **guinea pig** and 0.25 for **human**.

The *linear* path consists of a gain function followed by a cascade of three identical gammatone filters followed by a cascade of four Butterworth low pass filters. For both paths the cut-off frequency of the lowpass filters was set to the CF of the corresponding gammatone filters.

The CF of the nonlinear path gammatone filters ($CF_{Nl}$) is set to the desired BF of the filter as a whole, i.e. as a function of its location along the cochlear partition. The other parameters of the system are set relative to $CF_{Nl}$ using the formula:

$$log(parameter) = p0 + m\ log(CF_{Nl})$$

Table 1 shows the parameters *p0* and *m* values required to compute the parameters *a*, *b*, the bandwidths of both pathways ($BW_{lin}$ and $BW_{NL}$), the gain of the linear filter ($G_{lin}$), and the centre frequency of the linear filter ($CF_{lin}$).

| **DRNL filter parameters that vary with BF:** $p(BF) = 10^{p_0 + m\log_{10}(BF)}$ | Guinea pig | | human | |
|---|---|---|---|---|
| | p0 | m | p0 | m |
| Bandwidth of non-linear path, $BW_{NL}$ (Hz). | 0.8 | 0.58 | 0.1 | 0.783 |
| Compression parameter, *a* | 1.87 | 0.45 | 1.47 | 0.82 |
| Compression parameter, *b* | -5.65 | 0.875 | -2.674 | 0.358 |
| Center Frequency of linear path, $CF_{lin}$ (Hz). | 0.339 | 0.895 | 0.5 | 0.844 |
| Bandwidth of linear path, $BW_{lin}$ (Hz). | 1.3 | 0.53 | 0.097 | 1.185 |
| Linear path gain, $G_{lin}$. | 5.68 | -0.97 | 1.438 | -0.18 |

**Table 2. Coefficients for computing parameters of the DRNL filters as a function of $CF_{NL}$.**

## C. IHC receptor potential

Both guinea pig and human models used the same hair cell parameters (Sumner *et al.*. 2002, 2003a, 2003b). The displacement of the IHC cilia, *u(t)*, as a function of BM velocity, *v(t)*, is given by

$$\tau_c \frac{du(t)}{dt} + u(t) = \tau_c C_{cilia} v(t)$$

where $C_{cilia}$ is a gain factor and $\tau_c$ is a time constant. The cilia displacement causes a change in the in the apical conductance *G(u)*. The total apical conductance is given by:

$$G(u) = G_{cilia}^{\max}\left[1 + \exp\left(-\frac{u(t) - u_0}{s_0}\right)\left[1 + \exp\left(-\frac{u(t) - u_1}{s_1}\right)\right]\right]^{-1} + G_a$$

where $G_{cilia}^{max}$ is the transduction conductance with all channels open, and $G_a$ is the passive conductance in the apical membrane. $s_0$, $u_0$, $s_1$ and $u_1$ are constants determining the exact shape of the non-linearity. The membrane potential of the cell body is modeled with a passive electrical circuit analog:

$$C_m \frac{dV(t)}{dt} + G(u)\left(V(t) - E_t\right) + G_k\left(V(t) - E_k'\right) = 0$$

where *V(t)* is the intracellular hair cell potential; $C_m$ is the cell capacitance; $G_k$ is the voltage-invariant basolateral membrane conductance; $E_t$ is the endocochlear potential; and $E_k' = E_k + E_t R_p/(R_t + R_p)$ is the reversal potential of the basal current $E_k$ corrected for the resistance ($R_t$,$R_p$)of the supporting cells.

| | |
|---|---|
| Et, endocochlear potential (V) | 100e-3 |
| Ek, potassium reversal potential (V) | -70.45e-3 |
| G0, resting conductance (S= Siemens) | 1.974e-9 |
| Gk, potassium conductance (S) | 18e-9 |
| $E_k$ correction, Rp/(Rt+Rp) | 0.04 |
| $G_{cilia}^{max}$, max. mechanical conductance (S) | 8e-9 |
| $s_0$, displacement sensitivity ($m^{-1}$) | 85e-9 |
| $u_0$, displacement offset (m) | 7e-9 |
| $s_1$, displacement sensitivity ($m^{-1}$) | 5e-7 |
| $u_1$, displacement offset (m) | 7e-9 |
| $C_m$, total capacitance (F) | 15e-12 (6e-12) |
| $\tau_c$ cilia/BM time constant (s). | 2.13e-4 (2.13e-3) |
| $C_{cilia}$, cilia/BM coupling gain (dB) | 0 (16) |

**Table 3 IHC receptor potential. Values in brackets show original published values.**

## *D. Calcium controlled transmitter release function*

Depolarisation of the IHC membrane leads to an increase in the Calcium current ($I_{ca}$):

$$I_{Ca}(t) = G_{Ca}^{\max} m_{I_{Ca}}^3(t)\left(V(t) - E_{Ca}\right)$$

where $E_{Ca}$ is the reversal potential for calcium and $G_{Ca}^{max}$ is the calcium conductance in the vicinity of the synapse, with all the channels open. $m_{Ica}(t)$ is the fraction of calcium channels that are open. The steady state value of the latter, $m_{Ica,\infty}$, is modeled by a Boltzmann function,

$$m_{I_{Ca},\infty} = \left[1 + \beta_{Ca}^{-1}\exp\left(\gamma_{Ca}V(t)\right)\right]^{-1}$$

where $\beta_{Ca}$ and $\gamma_{Ca}$ are constants chosen to reflect published observations of calcium currents (see Table II), and $m_{Ica}(t)$ is a low pass filtered function of $m_{Ica,\infty}$

$$\tau_{I_{Ca}}\frac{dm_{I_{Ca}}(t)}{dt} + m_{I_{Ca}}(t) = m_{I_{Ca},\infty}$$

where $\tau_{Ica}$ is a time constant.

Calcium concentration $[Ca^{2+}](t)$ is modeled as a first-order low-pass filtered function of calcium current, $I_{Ca}(t)$:.

$$\tau_{[Ca]} \frac{d[Ca^{2+}](t)}{dt} + [Ca^{2+}](t) = I_{Ca}(t)$$

where $\tau_{[Ca]}$ is a time constant.

The probability of the release of transmitter is proportional to the cube of $Ca^{2+}$ concentration:

$$k(t) = \max\left(([Ca^{2+}]^3(t) - [Ca^{2+}]^3_{thr})z, 0\right)$$

where $[Ca^{2+}]_{thr}$ is a threshold constant, $z$ is a scalar for converting calcium concentration levels into release rate.

| | |
|---|---|
| z, scalar $(s*[Ca^{2+}]^3)^{-1}$) | 20e31 |
| $E_{Ca}$, reversal potential (V) | 0.066 |
| $\beta_{Ca}$ | 400 |
| $\gamma_{Ca}$ | 130 |
| $\tau_{m,,}$ calcium current time constant (s) | 1e-4 |
| $\tau_{Ca,}$ calcium diffusion time constant (s) | 1e-4 |
| $G_{Ca}^{max}$, max. $Ca^{2+}$conductance (nS) | 8e-9 |
| $[Ca^{2+}]_{thr}$ ($x10^{-11}$), threshold $Ca^{2+}$ conc. | 4.48e-11 |

**Table 4 Parameters for control of calcium levels.**

## *E. Quantal and probabilistic model of synaptic adaptation*

More detailed accounts of this process in a non-stochastic form can be found in Meddis (1986, 1988), Meddis *et al.* (1990) and Hewitt and Meddis (1991). The transmitter release rate, *k(t)*, drives a quantal model of synaptic adaptation that simulates the functional characteristics of adaptation, which are assumed here to be due to pre-synaptic transmitter depletion and is described by the following equations:

$$\frac{dq(t)}{dt} = N(w(t), x) + N([M - q(t)], y) - N(q(t), k(t)) \qquad (9)$$

$$\frac{dc(t)}{dt} = N(q(t), k(t)) - lc(t) - rc(t) \qquad (10)$$

$$\frac{dw(t)}{dt} = rc(t) - N(w(t), x) \qquad (11)$$

Individual vesicles of neurotransmitter (probably glutamate), are released from an *immediate pre-synaptic* (*q*) store into the *cleft* (*c*), at a rate, *k(t)*, that is dependent on calcium concentration. In the cleft, the transmitter disperses and some is lost from the system at a rate *l*. The remaining transmitter in the cleft is taken back into the cell into a *reprocessing* (*w*) store at a rate *r*. Here it is repackaged into vesicles that are returned to the immediate store at a rate *x*. Additionally, *q* is continuously replenished

with new transmitter vesicles at a rate, $y[M-q(t)]$ where $M$ represents the maximum number of transmitter quanta that can be held in the immediate store $(q)$.

Neurotransmitter in the immediate store is quantal, and enters and leaves stochastically. The stochastic transport of neurotransmitter is described by the function $N(n,\rho)$, in which each of $n$ quanta has an equal probability of release, $\rho dt$, in a single simulation epoch. In the cleft and reprocessing stores, transmitter is a continuous quantity. This means, for instance, that the contents of the reprocessing store must be an integer number greater than or equal to one for a transmitter quantum to be eligible to re-join the immediate store. The output from the synapse is a stream of discrete events indicating vesicle releases, $N(q(t),k(t))$.

| | |
|---|---|
| y, replenishment rate ($s^{-1}$) | 10 |
| l, loss rate ($s^{-1}$) | 2580 |
| x, reprocessing rate ($s^{-1}$) | 90 (66.3) |
| r, recovery rate ($s^{-1}$) | 6580 |
| M, max. free transmitter quanta | 10 |

**Table 5. IHC transmitter release parameters. Value in brackets is the previously published value.**

Initial values are found as follows:
c(0)= k(0)*y*m/(y*(l+r)+k(0)*l)
q(0)= c(0)*(l+r)/k(0)
w(0)=c(0)*r/x

## F. Auditory nerve response

15 auditory nerve fibers were used. The number of fibers firing in any given epoch was determined using a binomial distribution in association with random numbers. A refractory effect lasting 0.75 msec was applied. The width of each spike was 0.5 msec and it height was 9 arbitrary units.

## G. Sustained chopper model

This model is based on MacGregor's (1987) point neuron model. It consists of two stages; input at the dendrites and spike generation at the soma. The dendritic input stage applies a first-order low pass filter (3 dB cut-off at 300 Hz) to the train of input spikes to produce a representation of input current, $I(t)$ to the soma.

The trans-membrane potential at the soma is represented as a deviation from resting potential, $E_r$, and tracked using the equation:

$$dE(t)/dt= (-E(t) +\{[I(t)/G] + Gk(t)/G[Ek-E(t)]\}/)\tau m$$

where $\tau_m$ is the membrane time constant, $Ek$ is the potassium reversal potential (relative to $E_r$) and $Gk(t)$ is the cell potassium conductance:

$$dGk(t)/dt= [-Gk(t)+(b.s)]/ \tau_{Gk}$$

where $\tau_{Gk}$ is the potassium time constant, *b* is the increase in *Gk* following an action potential indicated when *s*=1. An action potential is initiated when the membrane potential exceeds a threshold *E(t)>Th0*. The threshold was fixed throughout.

| | |
|---|---|
| Membrane time constant τm (s) | 5e-4 |
| Potassium recovery time constant τ(Gk) (s) | variable |
| Increment in Gk on firing b | 0.1 |
| Resting threshold Th0 (mV) | 1.6 |
| Potassium reversal potential Ek (mV) | -10 |

**Table 6. MacGregor point neuron parameters.**

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