MODELLED PROPERTIES OF SINGLE NEURONS IN THE AUDITORY MIDBRAIN

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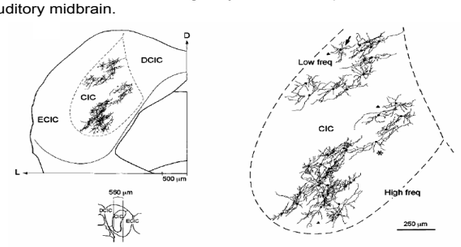
Introduction

In the auditory brainstem, information processed within the several parallel pathways that diverge from the cochlear nucleus converges again in the principal nucleus of the auditory midbrain, the inferior colliculus (IC). The output of the IC is the main source of input to the auditory thalamus and subsequently the auditory cortex. Thus, the inferior colliculus is a pivotal nucleus in the auditory pathway.

While the sources of projections to the IC are well established, we have little knowledge about how membrane properties and synaptic inputs combine in the IC to generate the responses of its neurons to sound.

Recordings of single neurons in the IC made *in vivo* and *in vitro* have identified their response patterns to sound stimulation or current injection (Le Beau et al 1996; Peruzzi et al 2000; Sivaramakrishnan and Oliver 2001). Up to six different response types have been identified, and *in vitro* studies suggest that the characteristics of the different cell types can be accounted for by activation of distinct types of potassium channels when they are exposed to different combinations of hyperpolarising and depolarising current injections (Sivaramakrishnan and Oliver 2001).

The aim of the current study is to use computational models to 1) determine whether the presence of the potassium channels identified *in vitro* are sufficient to generate the observed biological properties, and 2) to compare the responses of the modelled cells with the responses obtained from *in vitro* and *in vivo* recordings. The study is part of a larger project (MiCRAM) which aims to include these intrinsic properties of IC neurons in a biologically realistic computational and robotic model of the auditory midbrain.



A coronal section through the IC of the rat reveals its subdivisions (left). A *central nucleus* (CIC) is surrounded by two cortical-like areas, the *dorsal* (DCIC) and *external cortex* (ECIC). The CIC (right) has a characteristic laminar organization, which defines a tonotopical arrangement. Figure from Malmierca et al 1993.

Methods

Neurons were modelled using the GENESIS (Bower and Beeman 1997) modelling platform. The models consist of a somatic compartment whose dimensions (17 μm diameter) and membrane properties, e.g. resistance and capacitance, were based on measurements obtained from in vitro recordings (Sivaramakrishnan and Oliver 2001).

Sodium channels and a delayed rectifier potassium channel were included in all the modelled cell types. Other channels, such as the A-type potassium channel, were added when their presence had been identified from *in vitro* studies.

Simulated current injections like those used *in vitro* were used to test the models, and the channel densities were adjusted to generate response patterns that matched as closely as possible those obtained *in vitro*.

References

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Le Beau FEN, et al. (1996) Contribution of GABA- and glycine-mediated inhibition to the monaural temporal response properties of neurons in the inferior colliculus. *J Neurophysiol* 75: 902-919.

Malmierca MS et al. (1993) The central nucleus of the inferior colliculus in rat: a Golgi and computer reconstruction study of neuronal and laminar structure. *J Comp Neurol* 333:1-27.

Peruzzi D, et al. (2000) Identification of cell types in brain slices of the inferior colliculus. *Neuroscience* 101:403-416.

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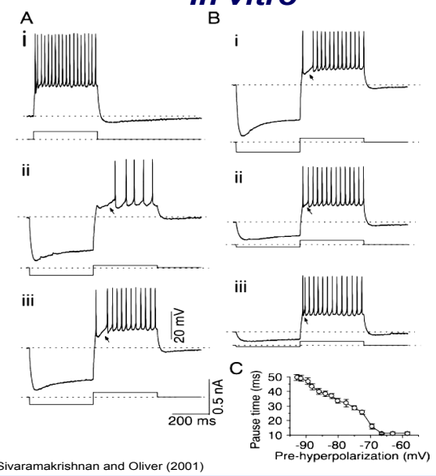
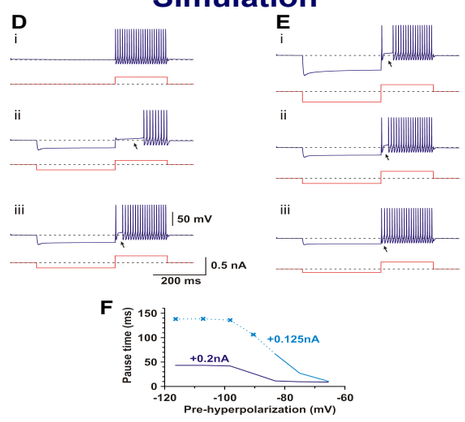
PAUSE-BUILD

In vitro



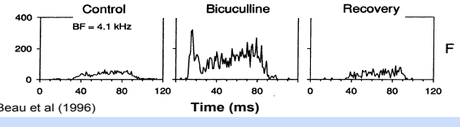
Sivaramakrishnan and Oliver (2001)

Simulation



Channel	Density
Sodium	1500
Potassium, delayed rectifier	30000
Potassium, A-Type	700
H-channel	2

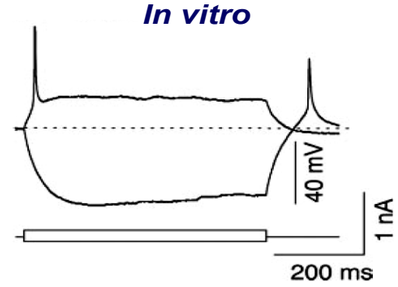
In vivo



Le Beau et al (1996)

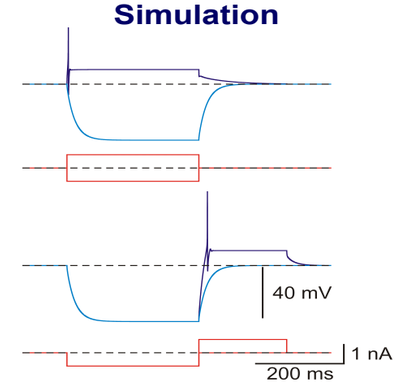
ONSET

In vitro



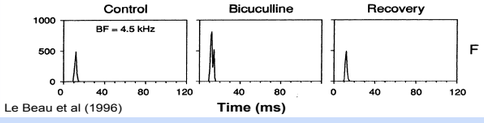
Sivaramakrishnan and Oliver (2001)

Simulation



Channel	Density
Sodium	2504
Potassium, delayed rectifier	21028

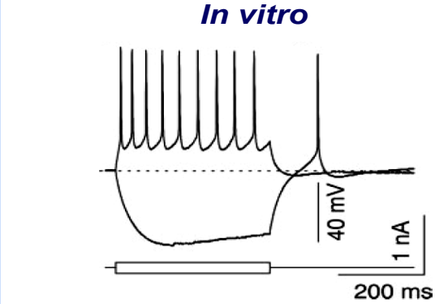
In vivo



Le Beau et al (1996)

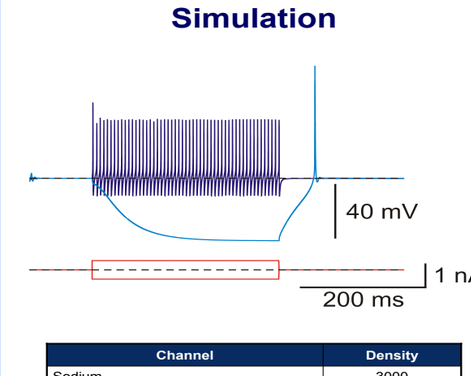
SUSTAINED-REGULAR

In vitro



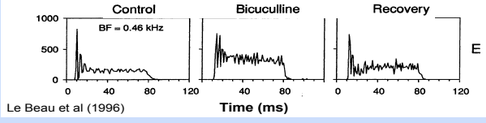
Sivaramakrishnan and Oliver (2001)

Simulation



Channel	Density
Sodium	3000
Potassium, delayed rectifier	16000
Calcium	2500

In vivo



Le Beau et al (1996)

Discussion

PAUSE-BUILD The distinctive pause-build response (Column 1) depends on the presence of an A-type potassium channel. **D**. In the absence of pre-hyperpolarisation the cell fires regularly (i). Hyperpolarisation applied prior to depolarisation activates the A-type channels. When this is followed by a weak depolarisation the cell fires with a build response (ii). Stronger depolarisation gives a pauser response (iii). **E**. The length of the pause depends on the prior hyperpolarisation, as shown in (**F**) where pause length is plotted versus pre-hyperpolarisation. An in vivo recording to sound, shows that blocking inhibition (hyperpolarisation) with bicuculline, converts a build response to a pauser.

ONSET The simulated onset response (Column 2) mimics the *in vitro* recording with a depolarising current injection, but the simulation does not generate an anode break spike following a hyperpolarising injection (pale blue line) unless it is accompanied by a depolarising injection (dark blue line). The *in vivo* recording demonstrates that inhibitory blockade does not change the response.

SUSTAINED-REGULAR The simulated sustained-regular response (Column 3) shows the same regular firing as the *in vitro* recording, although the spike rate of the simulation is higher. Like the real cell, the simulation fires an anode break-spike following a hyperpolarisation.

ACKNOWLEDGEMENTS Supported by EPRSC