Biological oscillators with autocatalytic steps: resonant release of synaptic transmitter

Daniel Andor-Ardó[1,2], A. J. Hudspeth[1], Marcelo O. Magnasco[2], and Oreste Piro[2,3]

***Short Abstract* — The auditory system is exquisitely frequency selective and is able to maintain temporal synchrony through early processing. We investigate ribbon synapses of auditory hair cells by means of a minimal model comprising a cycle of *N*-1 monomolecular steps and one autocatalytic step. Coöperativity pushes the system toward a Hopf bifurcation, enhancing frequency selectivity and synchronization. We demonstrate the basis of this improvement in the mass action limit, valid for large numbers of vesicles. We further compute the correction due to intrinsic fluctuations and show the phenomenon to be robust in the stochastic regime.**

***Keywords* — Ribbon synapse, coöperativity, Hopf bifurcation, synchronization, hair cell, fluctuations.**

I. Introduction

FREQUENCY selectivity and temporal synchronization are important in many dynamic biological systems. The auditory system in particular is exquisitely frequency selective and is able to maintain temporal synchrony through early processing [1]. Selectivity and fidelity come at great metabolic expense [2] and are supported by baroque morphological specializations. An instance of such a specialization is the ribbon synapse of the hair cell, essential for synchronous signaling [3].

II. Results

We investigate ribbon synapses of auditory hair cells by means of a minimal model. We show that in certain regimes coöperativity in the exocytotic release of neurotransmitter induces frequency selectivity and synchronization.

First, we characterize vesicle release at the synapse as an *N* step cycle; *N*=4 corresponds to a biologically plausible model of vesicle release. Although this cyclic process itself has some degree of resonance, we then show that coöperativity enhances resonance by pushing the eigenvalues toward the imaginary axis. Going through the resulting Hopf bifurcation brings with it the benefits of being near a dynamical critical point [4-6].

In the deterministic framework of the mass action limit, valid when the number of vesicle docking sites is large, we demonstrate the basis of this improvement. Intrinsic fluctuations due to the finite size of the more physiologically realistic stochastic regime bring corrections. Using an exact time-dependent Gillespie algorithm, we show that the phenomenon persists in the stochastic regime.

III. Conclusion

An oscillator based on a chain of monomolecular steps can be made arbitrarily resonant by the addition of a single autocatalytic feedback step. Using such an oscillator, we model the ribbon synapse. There is tantalizing evidence of frequency selectivity at the level of the hair-cell ribbon synapse [7]. We predict that coöperative vesicle release could therefore contribute to both frequency selectivity and synchronization at such synapses.

References

[1] Joris et al. (1994) Enhancement of neural synchronization in the anteroventral cochlear nucleus. I. Responses to tones at the characteristic frequency. *J. Neurophysiol.* **71**, 1022-36.
[2] Hudspeth (2008) Making an Effort to Listen: Mechanical Amplification in the Ear. *Neuron* **59**, 530-545.
[3] Khimich et al. (2005) Hair cell synaptic ribbons are essential for synchronous auditory signalling. *Nature* **434**, 889-94.
[4] Choe, Magnasco and Hudspeth (1998) A model for amplification of hair-bundle motion by cyclical binding of Ca^{2+} to mechanoelectrical-transduction channels. *PNAS* **95**, 15321-6.
[5] Camalet et al. (2000) Auditory sensitivity provided by self-tuned critical oscillations of hair cells. *PNAS* **97**, 3183-8.
[6] Ospeck, Eguíluz and Magnasco (2001) Evidence of a Hopf bifurcation in frog hair cells. *Biophysical Journal* **80**, 2597-2607.
[7] Rutherford and Roberts (2006) Frequency selectivity of synaptic exocytosis in frog saccular hair cells. *PNAS* **103**, 2898-903.

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[1]Howard Hughes Medical Institute and Laboratory of Sensory Neuroscience,
[2]Laboratory of Mathematical Physics, The Rockefeller University, 1230 York Avenue, New York, NY, 10065 6399 USA, and
[3]Institut Mediterrani d'Estudis Avançats, CSIC UIB, E 07071 Palma de Mallorca, Spain.