Extended dynamical range as a collective property of excitable cells

Osame Kinouchi
Departamento de Física e Matemática, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo
Av. dos Bandeirantes 3900, CEP 14040-901, Ribeirão Preto, SP, Brazil

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Abstract
Receptor cells with electrically coupled axons can improve both their input sensitivity and dynamical range due to collective non-linear wave properties. This mechanism is illustrated by a network of axons modeled by excitable maps subjected to a Poison signal process with rate \( r \). We find that, in a network of \( N \) cells, the amplification factor \( A \) (number of cells excited by a single signal event) decreases smoothly from \( A = \mathcal{O}(N) \) to \( A = 1 \) as \( r \) increases, preventing saturation in a self-organized way and leading to a Weber-Fechner law behavior. This self-limited amplification mechanism is generic for excitable media and could be implemented in other biological contexts and artificial sensor devices.

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1 Introduction
A very common trade-off problem encountered in the biology of sensorial mechanisms (and sensor devices in general) is the competition between two
desirable goals: high sensitivity (the system ideally should be able to detect even single signal events) and large dynamical range (the system should not saturate over various orders of magnitude of input intensity). In physiology, large dynamical ranges are related to Weber-Fechner law: the response $R$ of the sensorial system is proportional not to the input level but to its logarithm, $R \propto \ln I$.

Recently it has observed that synchronous activity on the olfactory epithelium suggest that receptor cells are electrically coupled, perhaps in the form of axo-axonal coupling [1]. Here we report a simple mechanism that could increase at the same time the sensitivity and the dynamical range of a sensory epithelium by using only this electrical axonal coupling. The resulting effect is transform the individual linear-saturating curves of individual cells into a collective Weber-Fechner-like logarithmic response curve with high sensitivity to single events.

Although the principles of self-limited amplification proposed in this work could be illustrated by using simpler elements (cellular automata), we have chosen to work with a system that model more realistically the dynamical behavior of biological cells. We represent each cell axon by a three variable discrete-time map which have a quasi-continuous behavior and reproduce spikes forms, bursts, adaptation to input and other biological phenomena. We hope that this more detailed approach improves the plausibility that the proposed mechanism really occur in the biological context.

The spiking behavior of various biophysical cell models is related to the presence of a saddle-node bifurcation in its fast variables subsystem [2]. For modeling excitable cells we propose to use a simple time-discrete map which also present a saddle-node bifurcation

$$
x(t+1) = \tanh \left( \left( x(t) - Ky(t) + Z + I(t) \right) / T \right), \\
y(t+1) = \tanh \left( \left( x(t) + H \right) / T \right).
$$

This map has two variables: the membrane potential $x(t)$ and the recovery variable $y(t)$. The external input is $I(t)$ and the model has four parameters $(T, K, Z, H)$. Phase diagrams for the parametric space can be found in [3]. With parameters $T = 0.3$, $K = 0.6$ and $H = -0.5$ the system has null-clines similar to the Morris-Lecar model [2]. There is a saddle-node bifurcation at $Z + I = Z_c$. If $Z > Z_c$ the cell presents repetitive firing without external
currents (pacemaker activity). At the border of this bifurcation ($Z < Z_c$), the cell behaves as an excitable element. In this case, we have repetitive firing above the critical current $I_c = Z_c - Z$ (Fig. 1a).

To model the adaptation phenomena usually present in receptor cells, we transform the parameter $Z$ into an endogenous adaptive current $z(t)$ so that the system is now a three variable map,

$$
x(t + 1) = \tanh \left[ (x(t) - K y(t) + z(t) + I(t)) / T \right],
$$

$$
y(t + 1) = \tanh \left[ (x(t) + H) / T \right],
$$

$$
z(t + 1) = (1 - \delta) z(t) - \lambda (x(t) - x_R). \quad (2)
$$

The adaptive current is a slow variable since $\delta, \lambda$ are small parameters. In the fixed point region, the equilibrium value $z^*$ is controlled by the reversion potential $x_R$: $z^* = \frac{\lambda}{\delta} (x_R - x^*)$ where $x^*$ is the resting membrane potential. As before, the system loses stability at $z^*_c + I = Z_c$.

Starting with a quiescent element (that is, $z^* < Z_c$), any external current $I > I_c$ will produce spikes with decreasing frequency (partial adaptation, see Fig. 1b) or even totally stop (total adaptation) depending on the ratio $\lambda / \delta$. Now the receptor cell response is adaptive: $z(t)$ adapts itself to counterbalance the effect of an external $I$ (Fig. 1c). After the external current is retired, the $z$ current returns to its original value with some decay time (adaptation and decay times are controlled by the parameters $(\delta, \lambda)$).

The relevant point here is that the two variable model $(x, y)$ has a small refractory time, but adaptive cells as the three variable model can have a very large refractory time. The refractory time is controlled by the $z(t)$ dynamics which decays after a spike and slowly grows afterwards (Fig. 2). This extended refractory time will be important for the dynamics of collective waves to be examined next.

The three dimensional model presents a variety of dynamical regimes on parameter space as excitable fixed points, excitable bursts, repetitive slow spiking, repetitive bursting, cardiac-like spikes etc. All this richness is essentially linked to the slow $z(t)$ dynamics which is also responsible for the adaptation to inputs $[3, 4]$. However, here we restrict our attention to a simple excitable regime where supra-threshold pulses induce only single spikes (with the large refractory time due to the $z$ dynamics).

Recently it has been suggested that receptor cells in the olfactory epithelium have their axons electrically coupled, perhaps by gap junctions $[4]$. 

3
Here we show that this electrical coupling could improve both the sensitivity and (at the same time) the dynamical range of receptor cells by using the formation and annihilation of collective waves.

Instead of a constant external current, suppose that the signal (say, the arriving of odorant molecules) is modeled by a Poisson process of supra-threshold events of stereotyped amplitude $i$: $I(t) = i \sum_n \delta(t - t_n)$ where the time intervals $t_{n+1} - t_n$ are distributed exponentially with rate $r$. The receptor cell response is shown in Fig. 3. Although the map has adimensional scales for time and membrane potential, the spike width of ten time steps provides a natural scale (biological spike widths are of order of 1 ms). In this figure we have used 10 time steps = 1 ms so that input and firing rates are given in 1/sec units. In the low rate regime the receptor cell activity is proportional to the signal rate. If the rate increases, there is a deviation from the linear behavior due to the refractory time $\Delta$ of the cell which, for the event amplitude used in the simulation ($i = 0.1$) is near $\Delta = 155$ time steps. For moderate input rates the response is well fitted by a linear-saturating curve for the firing rate:

$$f(r) = r/(1 + r\Delta),$$

which can be deduced from the fact that the firing rate is proportional to the rate discounting the refractory intervals, $f = r(1 - f\Delta)$. As one can see in Fig. 3, this saturation is not complete because two or more close events can be supra-threshold even if a single one is not (the refractory time is not absolute and there is temporal summation phenomena). This is already an interesting property of a single element because its dynamical range is larger than that predicted by Eq. (3).

How to improve the sensitivity for very low rates $r$? If we consider the response $R$ (spikes per second) of the total pool of $N$ independent cells, we have $R = Nf \approx Nr$, so increasing $N$ certainly increases the total sensitivity of the epithelium. Although certainly useful, this scaling is trivial since the efficiency of each cells remains the same.

Now, suppose that the cells axons are electrically coupled. Gap junctions are usually modeled as passive conductances between cell membranes,

$$I_{ij}^G(t) = \gamma_{ij} \left( x^i(t) - x^j(t) \right),$$

where $\gamma_{ij}$ is the gap conductance between cells $i$ and $j$. Here, for simplicity, we couple axon $x_j$ ($j = 1, \ldots, N$) to two neighbors with identical gap
conductances $\gamma$, in a one dimensional (transversal) geometry:

$$x_j(t+1) = \tanh \left( \frac{1}{T} (x_j(t) - K y_j(t) + z_j(t) + I_j(t) + \gamma [x_{j+1}(t) - x_j(t)] + \gamma [x_{j-1}(t) - x_j(t)]) \right),$$

$$y_j(t+1) = \tanh \left( \frac{(x_j(t) + H)}{T} \right),$$

$$z_j(t+1) = (1 - \delta) z_j(t) - \lambda (x_j(t) - x_R), \quad (5)$$

With $\gamma > 0.006$ one observes two waves propagating from a single excitation locus, a common phenomena in excitable media. These waves disappear at the extremes of the axon array because no periodic boundary conditions has been used. This means that a single event in only one of the receptor neurons is able to excite all the other axons, due to the propagating (transversal) wave [5]. Thus, the sensitivity per neuron has increased by a factor of $N$. This is a somewhat expected effect of the coupling: the axon of neuron $j$ excites even for events that arrive not at neuron $j$ but elsewhere in the network. More surprising is the fact that the dynamical range (the interval of rates where the neuron produces appreciable response) also increases dramatically (see Fig. 3).

This occurs due to a second effect (which we call the self-limited amplification effect). Remember that a single event in some neuron produces a total of $N$ axon responses. This is valid for small rates, where inputs are very isolated in time from each other. However, consider the case for higher signal rates where a new event occurs at neuron $k$ before the wave produced by neuron $j$ has disappeared. If the initiation site $k$ is inside the fronts of the previous wave, then two events produce $2N$ responses as before. But if $k$ is situated outside the fronts of the $j$-initiated wave, one of its fronts will run toward the $j$-wave and both fronts will annihilate (the other $k$ and $j$-fronts will continue until the borders) Thus, two events in the array have produced only $N$ axon excitations (that is, an average of $N/2$ per input event). So, in this case, the efficiency for two consecutive events (within a window defined by the wave velocity and the size $N$ of the axon array) is decreased by half.

If more events (say, $n$) arrive during a time window, diverse fronts co-exist but the average amplification of these $n$ events (how many axons each event excite) is only of order $N/n$. Since the number of coexisting waves is proportional to the input rate, we can estimate that the amplification factor
should decay in some range as the inverse of the rate $r$. The presence of large refractory times aids in the production of this scaling because new waves only can be created inside the wave fronts after the refractory time.

So, although the response for small rates is very high, saturation is avoided due to the fact that the amplification factor decreases with the rate in a self-organized way. In Fig. 3a we plot the amplification factor $A$ (firing rate of a coupled neuron divided by the firing rate of an isolated neuron for the same input rate). The amplification factor decreases in a sigmoidal way from $A = O(N)$ (for very small rates) to $A = 1$ where each cell responds as if isolated since waves have no time to propagate. The amplification factor sometimes exceeds $N$ because two or more consecutive waves may be produced by a single signal event. This explains the limit $A = 400$ for the $N = 200$ data and $A = 1600$ for the $N = 1000$ data in Fig. 3a.

If instead of sigmoidal the decreasing of $A$ were perfectly inverse $A = cN/r$, the system would adapt totally to the input rate. Inserting this $A$ factor in Eq. (3) gives $f(r) = rA/(1 + rA\Delta) = cN/(1 + cN\Delta)$ independent of $r$. The sigmoidal character of $A(r)$ gives the slow (Weber-Fechner-like) increase in the total response (Fig. 4a). Thus, a bunch of electrically coupled axons has a very interesting gain/dynamical-range curve which is a collective property not shared by individual, isolated axons. Due to the simplicity of the cell equations (and thus small computational times for each simulation), we can do a full study varying the array size $N$, neuron parameters, gap conductance values etc. These results are robust and will be fully reported elsewhere.

Recent experiments and computational work has focused on excitable waves and high frequency oscillations in axo-axonal electrically coupled cells in the hippocampus [6, 7]. We also have observed high frequency oscillations independent of input rate $r$ for a network of two-dimensional $(x, y)$ maps (reported in [3]). These oscillations also arise due the presence of gap junctions but, because the refractory time without the $z$ current is very small, an action potential in axon $i$ excites axons $i + 1$ and $i - 1$ which, by their turn, excite $i$ and so on: the oscillation frequency is determined by the latency time of this mutual excitation process, as suggested by Traub and co-workers [6].

Although the mechanism for generating excitable waves is studied in detail in [6, 7], no functional meaning for them is proposed (only some link to epileptic activity is discussed). However, since the hippocampus must be sensitive and at the same time not saturate due to the activity of other cerebral
areas which vary by orders of magnitude, the same self-limited amplification mechanism discussed here could be the primary function of axo-axonal coupling. Epileptic susceptibility would be an undesirable side effect of these electrically coupled networks when inhibitory influences (like the adaptive $z$ current) are shut off.

This mechanism for amplified but self-limited response due to wave annihilation seems to be a general property of excitable media and is not restricted to one dimensional systems. We conjecture that the same mechanism for increasing the dynamical range could be implemented at different biological levels, for example in the retina \cite{8} and in excitable dendritic trees in single neurons \cite{9}. This amplification mechanism could also be implemented in artificial detectors based in excitable media.

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**Figure 1:** a) Membrane potential $x(t)$ for the two variable system with parameters $T = 0.3, K = 0.6, Z = -0.13, H = -0.5$ and b) three variable system (adaptive cell) with parameters $T = 0.3, K = 0.6, H = -0.5, \delta = \lambda = 0.002, x_R = -0.98$; c) Evolution of slow variable $z(t)$ (solid bottom) for the adaptive cell: notice how $z(t)$ almost cancel the external current (solid top) injected at $t = 1000$ as can be seen in the curve $I + z$ (dots), producing a partial adaptation response.

**Figure 2:** a) Poisson distributed inputs $i = 0.1$ induce cell spikes if they occur out of the refractory cell time; b) Evolution of adaptive current $z(t)$. Notice that inputs $i(t)$ produce positive perturbations in $x(t)$ that, by its turn, produce negative perturbations in $z(t)$.

**Figure 3:** a) Amplification factor $A(r)$ and b) individual firing rate $f(r)$ in log-log plot for $N = 1000$ (circles) and $N = 200$ (triangles) coupled cells with $\gamma = 0.05$ compared to $N = 1000$ uncoupled cells (squares). The solid line for uncoupled cells is the linear-saturating function given by Eq. (3). Cell parameters as in Fig. 1b.

**Figure 4:** a) Individual firing rate in linear-log plot for $N = 1000$ coupled cells ($\gamma = 0.05$) (triangles) showing a quasi-logarithm behavior, $N = 1000$ uncoupled cells (squares) and linear saturating function (solid); b) Snapshot of coexisting waves ($\gamma = 0.05, N = 200$): $x(n)$ (membrane potential), $z(n)$ (slow current), $n = 1, \ldots, N$ is the axon index in the array. The first wave is moving to the right, the second wave is moving to the left and soon they will annihilate.
a) \[ I, z, I+z \]

b) \[ x \]

c) \[ l, z, l+z \]
a) $x(t), I(t)$

b) $z(t)$
