Return Map of a Periodically Driven Neuron

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RETURN MAP OF A PERIODICALLY DRIVEN NEURON

a thesis

by

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ABSTRACT

A typical neuron receives input from more than 10,000 other neurons. These inputs each get processed differently, depending on the neuron's morphology, chemistry, etc. The neuron may fire, in turn stimulating other nerve cells. The structure of a nerve cell determines the rules that govern the system but not the neuronal response. Also, the type of input affects the firing decision. Hence, a neuron can be viewed as a dynamical system and may be studied as such. The Hodgkin-Huxley model describes neuronal dynamics but this model is very complex. Here, I will study some simpler models in an attempt to determine what makes a neuron fire. In particular, I will ask: What is the effect of "rhythmic" impulses on a neuron?

Acknowledgements

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Dedicated to

My father, Robert Ambartsumyan, who can love unconditionally like no one I know.

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CHAPTER 1

Introduction

Unlike all the other cells in the human body, nerve cells, called **neurons**, are the only ones that carry electrical impulses. One cell passes a signal to another across **synapses**. In this way, neurons communicate with one another. To study this communication method, a neuron may be injected with a current. Currents might vary in frequency and could be injected over different time intervals. When a neuron receives such an input it either fires or not. If it fires, the result is generation of an **action potential** or **spike**. The question that one might ask is what happens inside a neuron when it receives an input? As it turns out, this is not a question with an easy answer. All we know is that once a neuron receives enough input to get activated it produces what, when graphed, appears like a spike. This spike means that the neuron fired. The spike may cause stimulation in other neurons, which in turn may or may not fire. The question is: What makes a neuron fire?

Before addressing this question we need to know some information about the chemistry of neurons. According to [**1**], electrical activity in neurons is sustained and propagated via ionic currents through neuron membranes. There are four basic types of transmembrane currents: sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-). The difference of concentrations of these ions on the inside and outside of the cell creates **electrochemical gradients**, the driving forces of neural activity. Proteins found in the cell membrane are channels through which the ions move. Each channel has a gating particle that activates or deactivates that channel. The gating particles are sensitive to the membrane potential, hence the channels are said to be **voltage-gated**. There are two kinds of currents: **persistent** (they do not inactivate the gates) and **transient** (they do inactivate the gates). If the equilibrium of a neuron is disturbed by an input, diffusion across the membrane helps the cell to recover. Now that we know what is going on inside a neuron, we can address the question of what makes it fire.

There have been many tests to try and understand what is going on inside the neuron when it receives a spike. It is known that once a neuron receives an input, it responds with **postsynaptic potentials** (**PSPs**). Some say that a neuron sums up PSPs and at a certain threshold it fires, but experiments show that this is not quite right. Evidently, when given the same input, neurons may respond with dramatic difference. Morphology of the neuron, the type of voltage, and Ca^{2+}-gated channels expressed by the neuron are certainly important, but these are just rules that determine neuronal response. Since neuronal dynamics could be studied in terms of activation and inactivation of voltage-gated channels, one can view a neuron as **nonlinear dynamical system**. The currents define what kind of dynamical system the neuron is. Different currents may results in the same rules and hence in the same responses. On the other hand, similar currents can result in different rules and in different responses. To understand the dynamical system of a given neuron one might try using equations to describe the spike generation mechanism.

As a matter of fact, Alan Lloyd Hodgkin and Andrew Huxley described such a mechanism, known as the **Hudgkin-Huxley model**. This model prefers inputs of certain frequencies that are similar to those of the subthreshold oscillations of a neuron; as such, it is called a resonator and it does not fire all-or-none spikes. This model consists of a set of differential equations in four variables. Three of these variables are called gating variables which represent voltage-gated ion channels that control the levels of persistent K^+ and transient Na^+ currents. Na^+ currents excite neurons so that they fire, whereas K^+ currents repolarize cells. The gates are voltage- and time-dependent. A neuron could be injected with a current over some period of time, or alternatively, current may be injected continuously or with frequent and short breaks between injections. During an experiment, a neuron might fire and, then, the goal is to determine at what point the neuron fired. However, the Hudgkin-Huxley model is very complicated and difficult to work with. It might be helpful to look at a simpler model, i.e. reduce this four dimensional system to a one-dimensional system called the Integrate-Fire model.

CHAPTER 2

Integrate-and-Fire models

A neuron whose membrane potential is resting is said to be at an **equilibrium point**. If we inject the neuron with a small current and it stays quiescent then the equilibrium is **stable**. Let V denote membrane potential and n denote activation variable, then as time is changing we can plot **trajectories** $(V(t), n(t))$ on the $V \times n$ - plane. These trajectories are depicted on a **phase portrait**. If a neuron is stable, then all trajectories converge to a point called an **attractor**. Small disturbances result in PSPs and large ones result in spikes. To understand the reason for a spike we must look at the region near the resting equilibrium, where the decisions to spike is being made. The transition from resting to sustained spiking is called **bifurcation**. Periodic spiking results in a **limit cycle** on the phase portrait. Neurons which undergo damped subthreshold oscillations when their equilibrium is disturbed are called **integrators**. Integrators integrate (response depends on the amount of current), resonators resonate (response depends on frequency). Thus, neurons fall into two categories: resonators and integrators. We would like to come up with simple model that resembles a neuron that integrates its dynamics. The desired model is called an **integrate-and-fire model** or **leaky integrate-and-fire model** (model that has Ohmic leakage current). Subthreshold behavior of such a neuron is described by the following equation:

$$C\dot{V} = I - \underbrace{g_{leak}(V - E_{leak})}_{\text{Ohmic leakage}}$$

where V is the membrane potential, I represents the injected current, $C\dot{V}$ is the capacitive current (the capacitance $C = 1.0\mu F/cm^2$), E_{leak} denotes leak reverse potential (potential at which the current reverses its direction), g_{leak} is the leak conductance and $(V - E_{leak})$ is the leak driving force. The neuron emits a spike whenever V is greater than or equal to the threshold value E_{thresh}. Note that V is a time-dependent variable but C, g_{leak} and E_{leak} are constant parameters. The above equation can be rewritten in dimensionless form as follows:

$$\dot{x} = b - x$$

The threshold value is $x = 1$, resting state is $x = b$, and reset value is $x = 0$. When $b < 1$ the neuron is in an excited state and fires periodic spikes when $b > 1$. The period of the system is $T = -\ln(1 - \frac{1}{b})$.

The integrate-and-fire model has some good neurocomputational properties but it also has some drawbacks. However, the drawbacks are not very significant for some one who wants to explore the model from a mathematical perspective. The good thing about the Integrate-and-Fire model is that it quantitatively captures the dynamics of a neuron.

CHAPTER 3

Constant Current with Periodic Term

I will now investigate the Integrate-and-Fire model of a neuron to study the effects of injecting a neuron with different types current. Specifically, I will be looking at some firing maps and come up with an equation that could be used to extract the input function. In this section T_{dr} denotes the period of the driving force, $I_0 + \phi(x)$ is some input signal, and $F(x)$ is the firing map. First, I will consider a differential equation having a periodic term. In the following equation I_0 is a constant current and $\phi(t)$ is a periodic term.

$$\dot{x} = f(x) + I_0 + \phi(t)$$

I would like to find the relationship between F and ϕ. Note that $\phi(t)$ is the periodic term i.e. $\phi(t+T_{dr}) = \phi(t)$. Solving the above differential equation will require finding an integrating factor.

$$\frac{dx}{dt} = -x + g(t)$$

$$x + \frac{dx}{dt} = g(t)$$

$$ux + u\dot{x} = ug$$

$$(ux)^{\cdot} = u\dot{x} + \dot{u}x$$

Find u s.t. $ux = \dot{u}x$ or $u = \dot{u}$. Let $u = e^t$.

$$(e^t x)^{\cdot} = e^t g(t)$$

$$(e^t x)^{\cdot} = e^t (I_0 + \phi(t))$$

Now I will integrate both sides of the above equation from t_0 (when $x = 0$) to $F(t_0)$ (when $x = 1$).

$$e^t x|_{t_0}^{F(t_0)} = \int_{t_0}^{F(t_0)} e^t (I_0 + \phi(t))dt$$

$$e^{F(t_0)} = \int_{t_0}^{F(t_0)} e^t (I_0 + \phi(t))dt$$

$$e^t = \int_{F^{-1}(t)}^{t} e^s (I_0 + \phi(s))ds$$

$$e^{F^{-1}(t)} = \int_{F^{-2}(t)}^{F^{-1}(t)} e^s (I_0 + \phi(s))ds$$

$$e^{F^{-2}(t)} = \int_{F^{-3}(t)}^{F^{-2}(t)} e^s (I_0 + \phi(s))ds$$

$$\vdots$$

$$\sum_{n=0}^{\infty} e^{F^{-n}(t)} = \int_{-\infty}^{t} e^s (I_0 + \phi(s))ds$$

Now the goal is to recover $\phi(s)$ from $F(t)$ by differentiating both sides of the above equation and solving for $\phi(t)$.

$$I_0 + \phi(t) = e^{-t} \left[\sum_{n=0}^{\infty} e^{F^{-n}}(t) \right]'$$

Lets now construct explicit $\phi(t)$ and $F(t)$ that satisfy the above equation.

Let $F(t) = t + C$

$F^{-1}(t) = t - C$

$F^{-1}(F^{-1}(t)) = F^{-1}(t - C) = t - C - C = t - 2C$

$F^{-1}(F^{-2}(t)) = t - 2C - C = t - 3C$

$\vdots$

$F^{-n}(t) = t - nC$

$\phi(t) = -I_0 + e^{-t} \dfrac{d}{dt} (\sum_{n=0}^{\infty} e^{F^{-n}}(t))$

$= -I_0 + e^{-t} \sum_{n=0}^{\infty} e^{t-nC}$

$= -I_0 + \sum_{n=0}^{\infty} e^{-nC}$

This is a geometric series. Since $|e^{-C}| < 1$,

$$\phi(t) = -I_0 + \frac{1}{1 - e^{-C}}$$

So we found the desired relationship between $\phi(t)$ and $F(t)$.

The next example will be constructed via Mobius transformations, which preserve circles and angles. Specifically, these maps preserve the unit circle ($|z| = 1$). The following Mobius transformation is a special type having three real dimensions:

$$S(z) = \rho\frac{z - \alpha}{1 - \bar{\alpha}z}, \ \ |\rho| = 1, |\alpha| < 1$$

Let $\Phi : \mathbb{R} \to S$ be the map s.t. $\Phi(x) = e^{2\pi i x}$. I would like to find a map $\tilde{S} : \mathbb{R} \to \mathbb{R}$ s.t. the following diagram commutes.

$$\begin{array}{ccc} \mathbb{R} & \xrightarrow{\Phi} & S^1 \\ \downarrow{\scriptstyle \tilde{S}} & & \downarrow{\scriptstyle S} \\ \mathbb{R} & \xrightarrow{\Phi} & S^1 \end{array}$$

In the diagram above S^1 is the unit circle and $S(z)$ is the Mobius transformation. To find the expression for $\tilde{S}$ if suffices to solve for it in the following expression (letting $\rho = 1$ for simplicity):

$$e^{2\pi i(\tilde{S}(x))} = \frac{e^{2\pi i x} - \alpha}{1 - \bar{\alpha}e^{2\pi i x}}$$

Solving for $\tilde{S}(x)$ we get:

$$\tilde{S}(x) = \frac{1}{2\pi i} \ln \left(\frac{e^{2\pi i x} - \alpha}{1 - \bar{\alpha} e^{2\pi i x}} \right)$$

Consider the special case $\alpha = a, 0 \leq a < 1$. Let

$$\begin{aligned} y &= -i \ln \left(\frac{e^{2\pi i x} - a}{1 - a e^{2\pi i x}} \right) \\ &= -i \left(Re \ln \left(\frac{e^{2\pi i x} - a}{1 - a e^{2\pi i x}} \right) + i Im \left(\ln \frac{e^{2\pi i x} - a}{1 - a e^{2\pi i x}} \right) \right) \\ &= Im \left(\ln \frac{e^{2\pi i x} - a}{1 - a e^{2\pi i x}} \right) \end{aligned}$$

In order to express $\frac{e^{2\pi i x} - a}{1 - a e^{2\pi i x}}$ in the form $u + iv, u, v \in \mathbb{R}$, we multiply both sides of this expression by its conjugate:

$$\begin{aligned} u + iv &= \frac{e^{2\pi i x} + a}{1 + a e^{2\pi i x}} \\ &= \left(\frac{e^{2\pi i x} + a}{1 + a e^{2\pi i x}} \right) \left(\frac{1 + a e^{-2\pi i x}}{1 + a e^{-2\pi i x}} \right) \\ &= \frac{e^{2\pi i x} + 2a + a^2 e^{-2\pi i x}}{1 + a(e^{-2\pi i x} + e^{2\pi i x}) + a^2} \\ &= \frac{(1 + a^2)\cos(2\pi x) + 2a + i(1 - a^2)\sin(2\pi x)}{1 + 2a\cos(2\pi x) + a^2} \end{aligned}$$

So

$$u = \frac{(1+a^2)\cos(2\pi x) + 2a}{1 + 2a\cos(2\pi x) + a^2}$$

and

$$v = \frac{(1-a^2)\sin(2\pi x)}{1 + 2a\cos(2\pi x) + a^2}$$

Hence,

$$\begin{aligned}
\tan(\frac{v}{2}) &= \frac{\frac{(1-a^2)\sin(2\pi x)}{1+2a\cos(2\pi x)+a^2}}{1 + \frac{(1-a^2)\cos(2\pi x)+2a}{1+2a\cos(2\pi x)+a^2}} \\
&= \frac{(1-a^2)\sin(2\pi x)}{1 + a^2 + 2a\cos(2\pi x) + (1+a^2)\cos(2\pi x) + 2a} \\
&= \frac{(1-a^2)\sin(2\pi x)}{(1+a)^2\cos(2\pi x) + (1+a)^2}
\end{aligned}$$

and $\tan(\frac{v}{2}) = \frac{1-a}{1+a}\tan(\frac{2\pi x}{2})$. Solving for v,

$$v = 2\arctan\left[\tfrac{1-a}{1+a}\tan(\tfrac{2\pi x}{2})\right].$$

Let $S_r(x) = \frac{1}{\pi}\arctan\left[r\tan(\pi x)\right]$

The firing map is $F_r(x) = S_r(x) + k, 0 \leq x \leq 1, k \in \mathbb{N}$.

Extend using $F_r(x+1) = F_r(x) + 1$. The nth iterate is given by $F_r^n(x) = S_{r^n}(x) + nk$ for $n \in \mathbb{Z}$.

Letting

$$
\begin{aligned}
S_r(x) &= S_{r^n}(x) \\
F_r^n(x) &= S_{r^n}(x) + nk \\
F_r^{-n} &= S_{r^{-n}}(x) - nk \\
&= \frac{1}{\pi}\arctan(r^{-n}\tan(\pi x)) - nk
\end{aligned}
$$

I would like to use this firing map to recover the original input function $\phi(x)$ for this firing map. To accomplish this task I will use the equation that I derived earlier in this paper which relates $\phi(x)$ and F.

$$
I_0 + \phi(x) = e^{-x}\left(\sum_{n=0}^{\infty} e^{F_r^{-n}(x)}\right)'
$$

where $F_r^{-n}(x) = \frac{1}{\pi}\arctan(r^{-n}\tan(\pi x)) - nk$. The input function

$$
I_0 + \phi(x) = 2\pi e^{-x}\sec^2(\pi x)\sum_{n=0}^{\infty}\frac{e^{2\tan^{-1}(r^{-n}\tan(\pi x))}e^{-nk}}{r^n + r^{-n}\tan^2(\pi x)}
$$

is very complicated. Instead of trying to simplify it, I will study it in order to figure out its behavior. I am particularly interested in its behavior at the origin for various values of r. Let

$$g(x) = \sum_{n=0}^{\infty} e^{-n} e^{\frac{1}{\pi}\tan^{-1}(r^{-n}\tan(\pi x))}$$

$$f(x) = e^{-x} g'(x)$$

$$f(0) = \sum_{n=0}^{\infty} (er)^{-n}$$

$$\begin{aligned} f'(0) &= g''(0) - g'(0) \\ &= \sum_{n=0}^{\infty} e^{-n}(r^{-2n} - r^{-n}) \\ &= \sum_{n=0}^{\infty} (er^2)^{-n} - (er)^{-n} \end{aligned}$$

When $e^{-\frac{1}{2}} < r < 1$, both $\phi(0)$ and $\phi'(0)$ are finite. See Figure 1 for the graph of $\phi(x)$ when $r = 0.83$.

When $e^{-1} < r < e^{-\frac{1}{2}}$, $\phi(0) < \infty$ but $\phi'(0) = \infty$. See Figure 2 for the graph of $\phi(x)$ and Figure 3 for the graph of $\phi'(x)$ when $r = \frac{1}{2}$.

When $0 < r < e^{-1}$, both $\phi(0)$ and $\phi'(0)$ are infinite. See Figure 4 for the graph of $\phi(x)$ when $r = 0.2$.

We find that critical value of r for which $\phi'(x) = \infty$ is $r_c = e^{-\frac{1}{2}} \approx 0.61$. Also, as the value of r decreases from around 1 to 0, the graph of $\phi(x)$ becomes infinite.

One of the results that was achieved in this paper is derivation of the equation that relates an input function to the firing map. Using this equation one can look at any firing map and figure out the input signal.

Second result is achieved through the use of the equation that relates the firing map and the input function. I chose a firing map that was periodic and recovered the input signal. Properties of the input function were described above for various values of r.

CHAPTER 4

Conclusion

Neurons exhibit different dynamics so there are many ways to model them. In this paper I studied the simplest model of a neuron called "integrate and fire." While studying this model I derived the equation that relates the firing map of a neuron and its input signal. Then I used a specific firing map to reconstruct the input signal for the firing map. I found that as we vary the derivative of the return map at its attracting fixed point from 1 to 0, the input signal first develops infinite slope and then becomes infinite itself at $t = 0$. So thus the return map cannot be too strongly attracting at its fixed point without the input signal blowing up. In the future, I hope to study this phenomenon in more complex neural models such as two-dimensional voltage/gating models, and more broadly, continue to research the question of how a neuron's firing pattern can be used to decode its input signal.

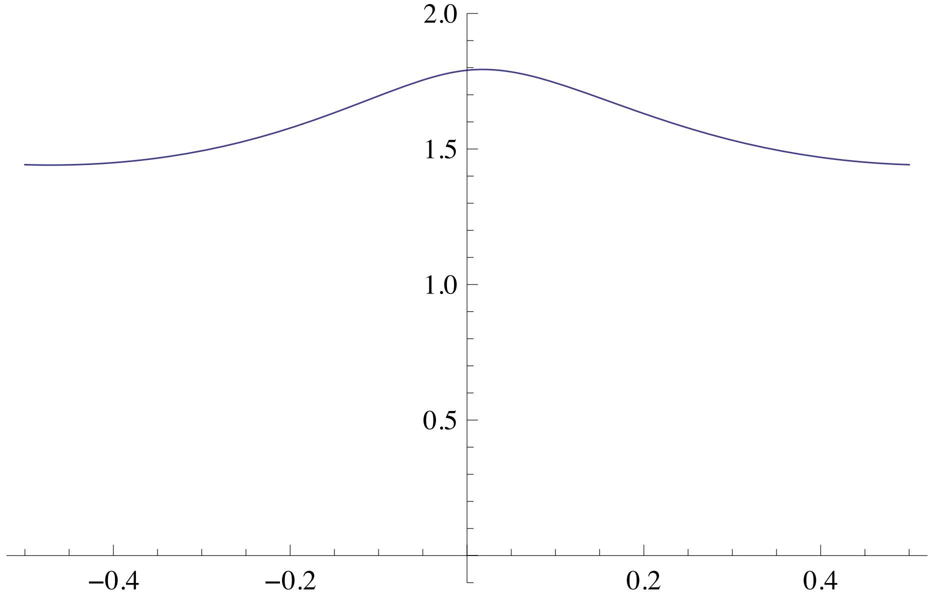

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FIGURE 1. Graph of $\phi(x)$ when $r = 0.83$

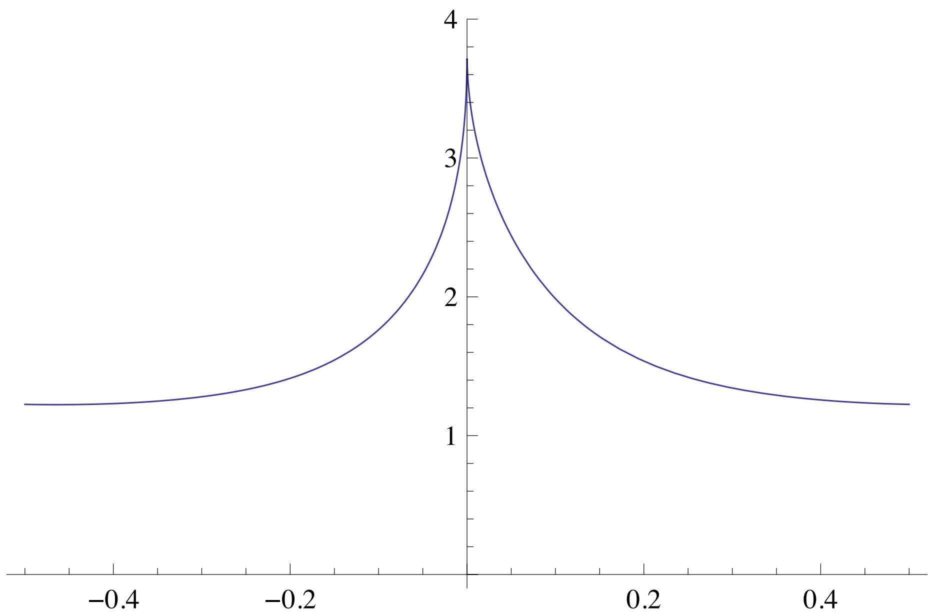

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FIGURE 2. Graph of $\phi(x)$ when $r = \frac{1}{2}$

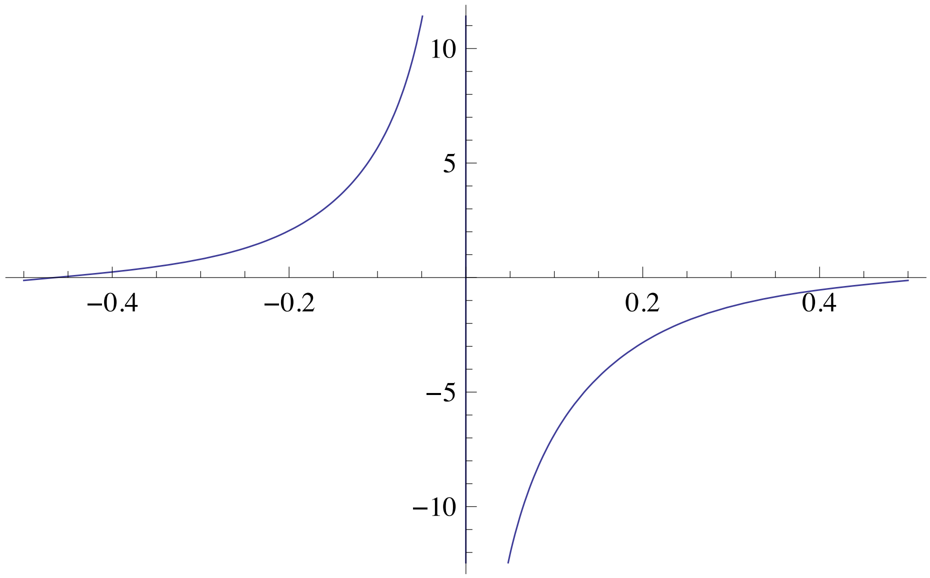

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FIGURE 3. Graph of $\phi'(x)$ when $r = \frac{1}{2}$

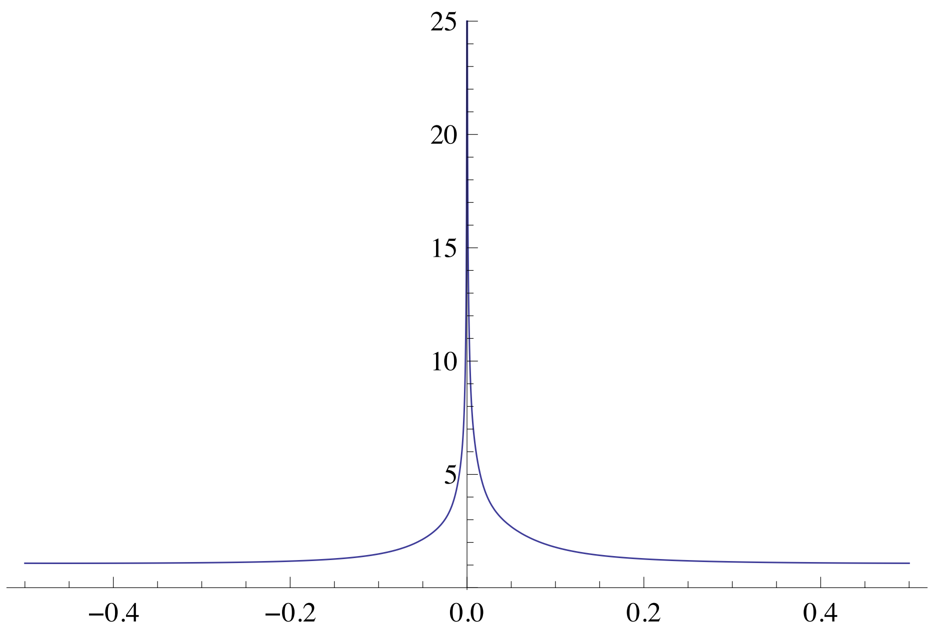

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FIGURE 4. Graph of $\phi(x)$ when $r = 0.2$

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[1] Eugene M. Izhikevich *Dynamical Systems in Neuroscience* 2007.