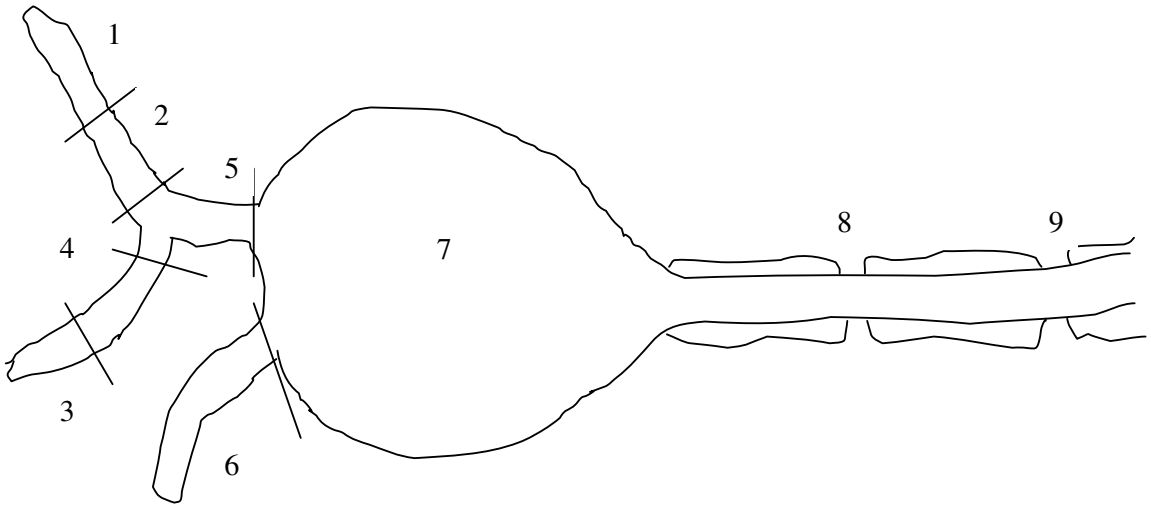
16-10-2007

SOMATODENDRITIC SIGNAL PROCESSING

(SpatioTemporal Mapping)

A hypothetical case study:

Each section of the dendrites (1,2,3,4,5,6), the soma (7) and the Nodes-of-Ranvier (8,9,...) can be modeled by membrane models connected by internal resistances. For simplicity, outside resistances can be taken to be zero and the whole of the outside solution may be taken as the reference voltage i.e. the common ground.



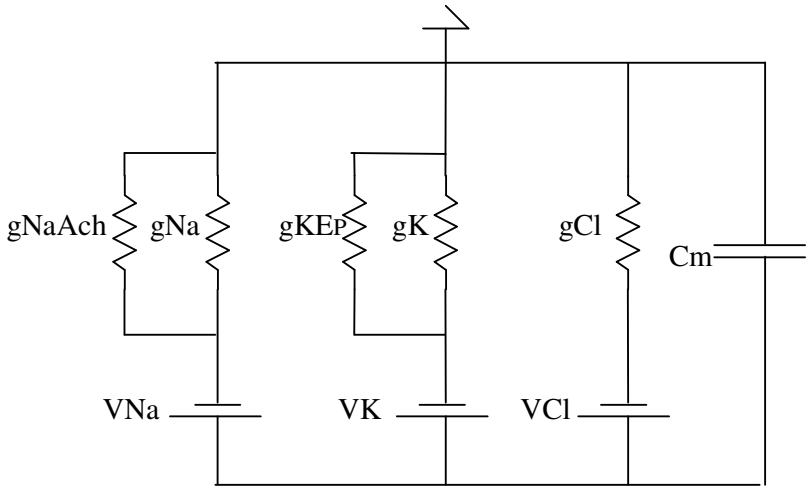
Note that dendritic extensions are like cylinders and their radii decrease towards their ends. Forexample we can consider the following parameters:

Section	radius (μm)	length (cm)
1	2	0.03
2	3.15	0.0365
3	2	0.03
4	3.15	0.0365
5	5	0.046
6	5	0.046

For the soma we can consider a large body having a surface area equivalent to a cylinder of radius 8 μm and length 0.1 cm. The Node-of-Ranviers could be modelled by cylinders of radii 2 μm and lengths 0.003 cm. Note that the nodes are very short because this is the length of the unmyelinated section. The length of the myelinated section can be taken as 50 times longer, i.e. equal to 50 X 0.003 = 0.15 cm.

In addition one can take σ_{inside} = 8 mS/cm and c_m = 0.9444 F/cm^2 .

The dendritic and somatic membranes (1,2,3,4,5,6,7) are not excitable i.e. they do not have voltage-dependent conductances but they have fixed conductances and additional neuro-transmitter sensitive conductances for Na and K as shown below.



We can use the following values:

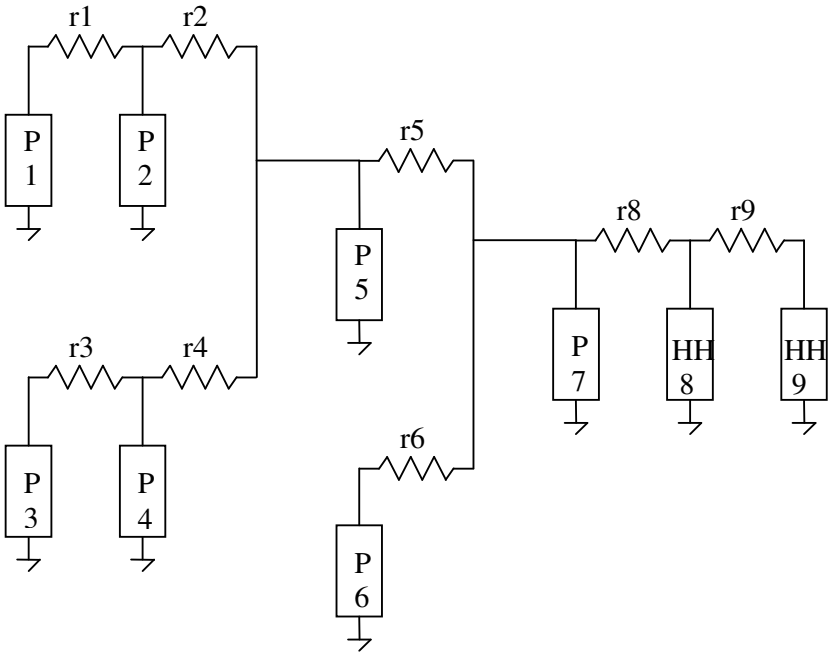
gNa = 0.0036 mS/cm^2 , gK = 0.12 mS/cm^2 , gCl = 0.1 mS/cm^2
VNa= 45 mV, VK = -82 mV, VCl = -59.4 mV

Note that these values correspond to -70 mV membrane voltage assuming that neurotransmitter conductances are zero. With the arrival of a presynaptic AP to section 1 forexample we may assume that gNaAch of that section becomes 500 X gNa for 2 mseconds. Similarly for a synapse which is using Epinephrine one can assume a similar behavior for GKEp.

The membrane models of Node-of-Ranviers (nodes) are of H-H type and the following parameters can be assumed:

gNamax = 180 mS/cm^2 , gKmax = 36 mS/cm^2 , gCl = 0.3 mS/cm^2
gNa = gNamax*m^3*h, gK = gKmax*n^4
Resting values for n,m,h are as 0.3177, 0.05293, 0.5961 respectively.
With these values, at rest, the membrane potential is -70 mV again.

The whole circuit is as follows where the membrane section blocks are turned upside down so that the ground is at the bottom. Here the blocks labeled by P are passive in that they do not have membrane voltage dependent conductances and therefore cannot have APs. The sections labeled by HH are active and can generate Aps. The resistances r_1,r_2,… ,r_6 are the axoplasmic resistances of the cylindrical dendritic sections. There is no r_7 because the soma is quite thick. r_8 is the resistance connecting the soma to the 1st node, and r_9 connects the 1st and 2nd nodes. Only two sections of the axon are taken.



We can calculate the parameters of the different sections as

Section	Cm(microF)	GNa_rest (mS)	GK_rest (mS)	r (Kohms)	GCl (mS)
1	35.6×10^{-6}	0.136×10^{-6}	4.52×10^{-6}	29.84×10^{3}	3.77×10^{-6}
2	68.2×10^{-6}	0.26×10^{-6}	8.67×10^{-6}	14.64×10^{3}	7.22×10^{-6}
3	35.6×10^{-6}	0.136×10^{-6}	4.52×10^{-6}	29.84×10^{3}	3.77×10^{-6}
4	68.2×10^{-6}	0.26×10^{-6}	8.67×10^{-6}	14.64×10^{3}	7.22×10^{-6}
5	13.65×10^{-6}	0.52×10^{-6}	1.734×10^{-6}	7.32×10^{3}	14.45×10^{-6}
6	13.65×10^{-6}	0.52×10^{-6}	1.734×10^{-6}	7.32×10^{3}	14.45×10^{-6}
7	47.47×10^{-6}	1.81×10^{-6}	6.032×10^{-6}	---	50.27×10^{-6}
8*	0.36×10^{-6}	678.6×10^{-6}	135.7×10^{-6}	149.21×10^{3}	1.13×10^{-6}
9*	0.36×10^{-6}	678.6×10^{-6}	135.7×10^{-6}	149.21×10^{3}	1.13×10^{-6}

* : Gna_max and GK_max are reported instead of GNa_rest and GK_rest respectively.

In the neuron model we are using, since we assume that sections 1-7 do not have voltage dependent conductances and that they cannot generate APs, the first section which generates AP is section 8, and this AP propagates outward along the axon of the neuron. Therefore we consider the AP frequency at node (section) 8 as the output of our model neuron. The inputs are the AP frequencies of presynaptic neurons. In general the output frequency generated at node 8 is related to the average level of membrane potential at the soma (section 7). Thus input APs coming from the presynaptic cells contribute with different weights to the formation of a DC voltage (with ripple) at 7. The higher this voltage is, the higher is the output frequency.

We can generate A Matlab code which models this neuron and use this code to perform different experiments:

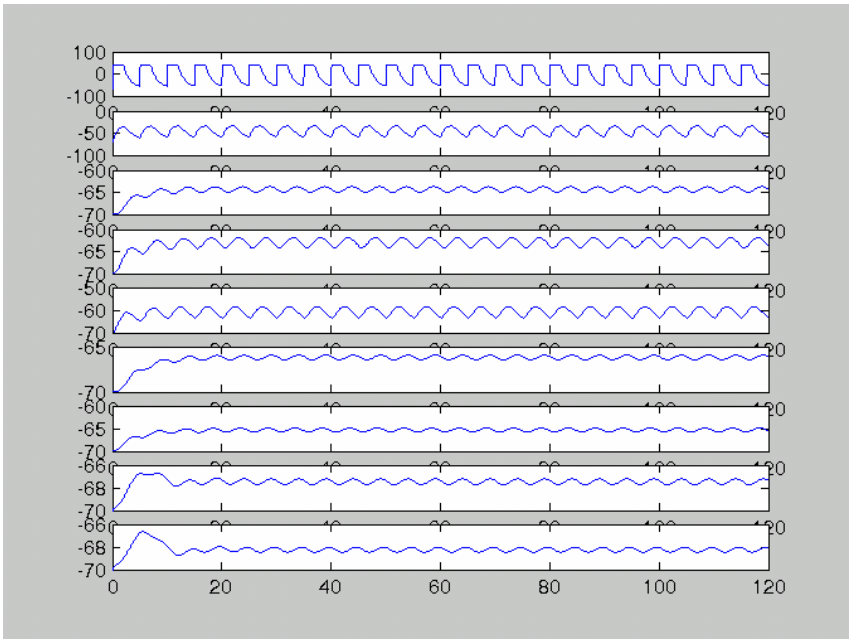
a) Assume a presynaptic AP train arrives at section 1 with frequency f and each AP changes gNaAch of section 1 from zero to KxGna_rest for 2 mseconds. Observe and plot Vm at all sections. What is the maximum output AP frequency obtained at section 8? Assume that K cannot exceed 5000 and f cannot exceed 200 spikes/second (APs/sec).
b) Repeat a) for section 4. In other words presynaptic APs arrive at section 4.
c) Repeat a) for section 6. Obtain a table which tabulates output frequency for different f and K values such as

	f = 200	f = 100	f = 50
K = 5000			
K = 4000			
K = 3000			
K = 2000			
K = 1000			
K = 500			
K = 200			
K = 100			

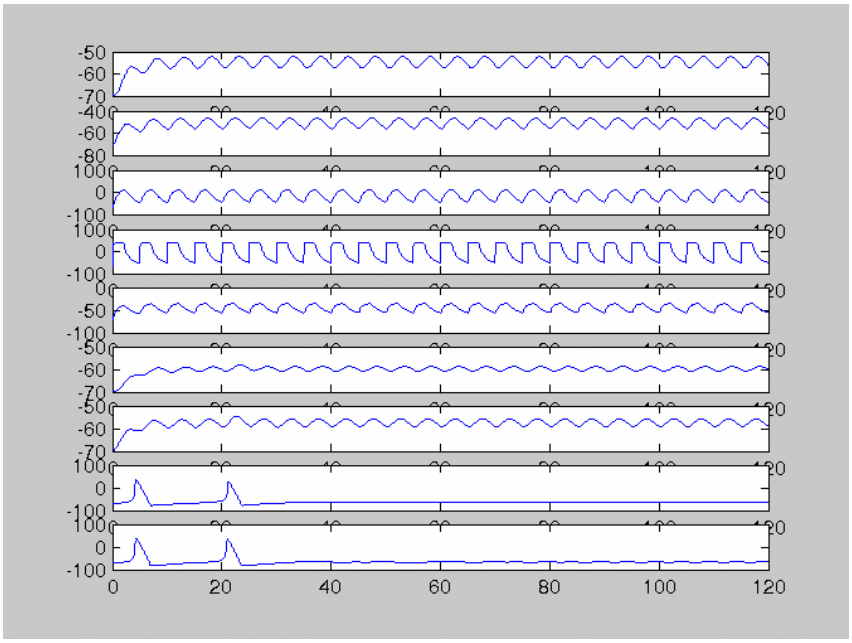
d) Assume sections 1 and 4 are simultaneously excited. Is there any advantage? Show by an example.
e) Show how section 4 can modulate the effect of section 6 by an example.
f) Assume 1 and 4 are excitatory as before but 6 is inhibitory. Inhibitory may mean that at section 6 the neurotransmitter is not AcH but forexample Epinephrine (EP). The effect of EP may be taken as that GKEP becomes 4 x GK_rest for 2 msec at each AP. Demonstrate by an example how 6 effects the response to combined stimulation of 1 and 4.

Results of the experiments are given below. In the following graphs there are 8 curves which are Vm1, Vm2, …, Vm9 from top to bottom.

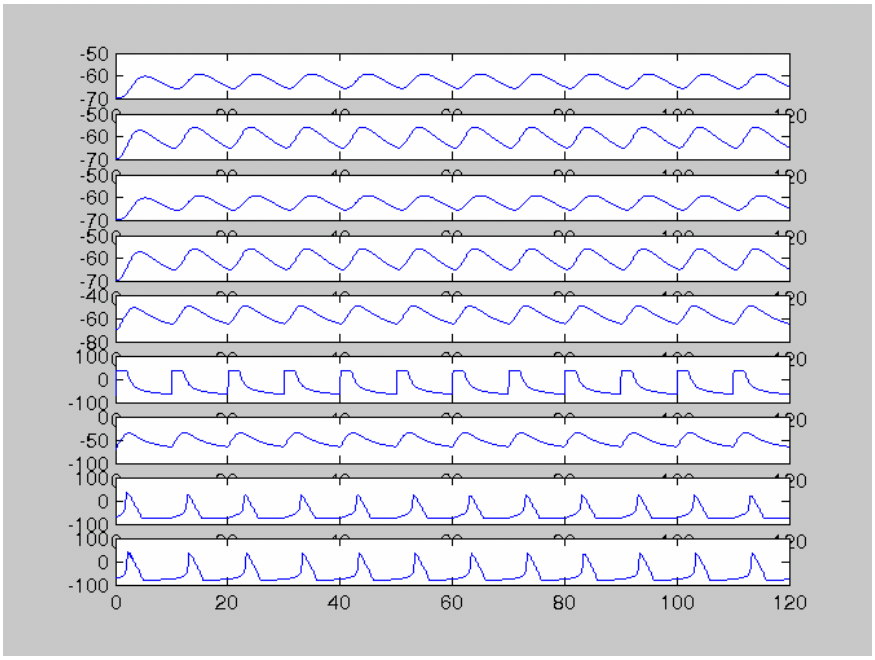
a) Even if K = 5000 and f = 200 are selected, APs are not generated in the axon. That is maximal stimulation at section 1 is not sufficient to elicit APs.



b) Same is true for section 4. Although two APs are generated we do not obtain a continuous stream of APs and the output frequency is still zero.



c) Stimulation at section 6 with K = 4000 and f = 100 we get an output frequency of 100 spikes/sec.

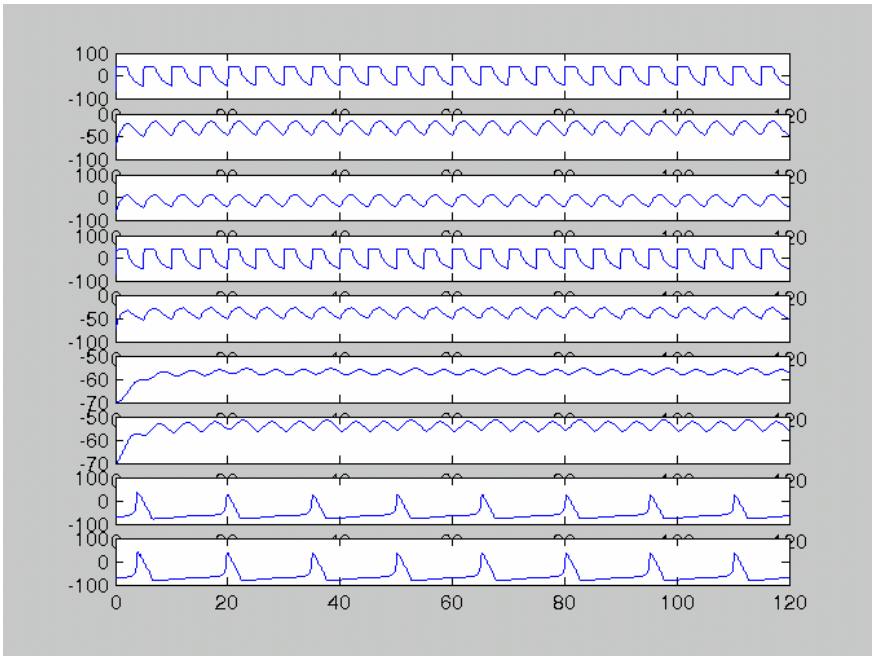


Output frequency with respect to K and input f.

	f = 200	f = 100	f = 50
K = 5000	100	100	50
K = 4000	100	100	50
K = 3000	100	100	50
K = 2000	100	100	50
K = 1000	89	81	50
K = 500	79	66	50
K = 200	65	50	50
K = 100	0	49	50

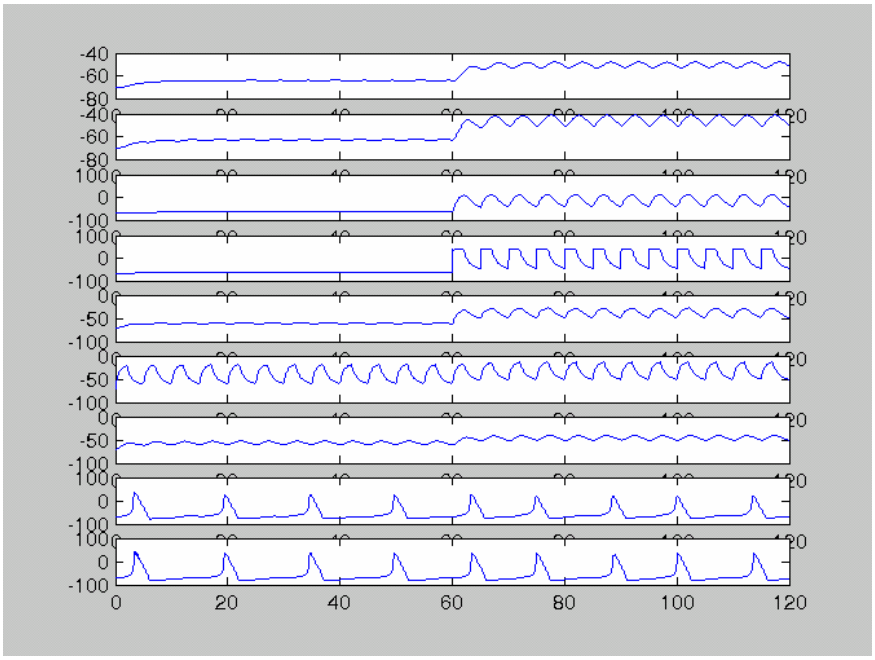
Thus as K is decreased ouput frequency decreases but it cannot be less than around 50. In one case it is zero. Similarly for a fixed K as f is decreased output frequency decreases.

d) If 1 and 4 are maximally excited we get an output frequency of 66 spikes/sec. This means that 1 or 4 is not sufficient to generate a nonzero output frequency by itself but together they can.



If 4 is stimulated maximally but 1 is stimulated submaximally (K=50 f = 200 forexample) then output frequency is 60 s/s. That is 1 can modulate the effect of 4 and also it can be shown that 4 can modulate the effect of 1.

e) Example: 6 is stimulated with K=200 and f =200 between 0 and 120 msec.
4 is stimulated with K=5000 and f=200 between 60 and 120 msec.
Between 0 and 60 msec output freq is 66 s/s and between 60 and 120 msec it is 77 s/s.
Therefore by changing stimulation at 4 we can modulate the effect of stimulation at 6.



f) 1 and 4 are stimulated maximally between 0 and 120 msec. 6 is stimulated with K = 4 (for potassium) and f =200 starting at 60 msec and up to 120 msec. We find that due to the inhibitory effect of 6, the output frequency decreases to 50 s/s from 63 s/s starting at 60 msec.