Computing Conditional Probabilities in a Minimal CA3 Pyramidal Neuron

Ashlie B. Hocking and William B Levy

Department of Neurosurgery, University of Virginia Health System, P. O. Box 800420 Neursurgery

Charlottesville, VA 22908-0420, USA

Abstract

The function of the CA3 region of the hippocampus can be explained in terms of a sequence predicting recoder. For the CA3 to act as a neural prediction device, each CA3 neuron must also act as a predictor. Thus, such neurons, as prediction devices, compute something that might approximate a conditional probability. In particular, we conjecture that each neuron forecasts its own firing. Here we compare a simple neural network model, based on synaptic encoding of local conditional probabilities to an even simpler model of hippocampal region CA3 that succeeds on a variety of hippocampally dependent learning tasks.

Keywords: Hippocampus; McCulloch-Pitts; Conditional Probability; Forecasting; CA3

1. Introduction

The treatment of the hippocampus as a sequence prediction device incorporates most existing explanations of its purpose [2]. As a sequence prediction device, the hippocampus can forecast what will happen next if the input is sufficiently similar to a previously encountered input. Within the hippocampus, the CA3 region is

paramount in this forecasting ability, while other regions help to recode the input and decode the output [2].

In the conditional probability based model for the hippocampus, the CA3 region generates the probability that a particular event will occur in the immediate future, given that a particular sequence of events has just occurred. The firing pattern of the CA3 encodes this probability, based on external input from the entorhinal cortex and dentate gyrus, as well as recurrent input from within the CA3 itself, which provide information regarding previous events. One method of decoding a CA3 forecast [1] assumes that a CA3 pyramidal neuron that fires when an event occurs also fires as a signal that the same event is expected to occur.

In one model of the CA3 region [6], each pyramidal neuron receives input from both an external source (corresponding to the entorhinal cortex and dentate gyrus) and recurrently from each other. In this model, the neuron fires if it receives an external input or a sufficiently strong recurrent input. Specifically, the internal activation due to recurrent input is modeled as

$$y_j(t) = \frac{\sum_{i=1}^{n} w_{ij} z_i(t - \Delta t)}{\sum_{i=1}^{n} w_{ij} z_i(t - \Delta t) + K_{FB} \sum_{i=1}^{n} z_i(t - \Delta t) + K_{SH} + K_{FF} \sum_{i=1}^{n} x_i(t)}, \qquad (1)$$

where w_{ij} represents the strength of the synapse from neuron i to neuron j, $z_i(t-\Delta t)$ is a binary variable representing whether neuron i fired in the previous computational interval, x_i is a binary input indicating whether neuron i received external forcing input, and K_{FB}, K_{SH}, and K_{FF} are coefficients of the feedback, shunting, and feedforward inhibitions, respectively [2]. In this model, neuron j fires if either $y_j(t) > \theta$ (where θ is typically one-half), or if it receives external forcing input.

By contrast, starting from a model based entirely on conditional probabilities, an equation similar to equation 1 can be derived:

$$y_j(t) = \frac{\sum_{i=1}^{n} v_{ij} z_i (t - \Delta t)}{\sum_{i=1}^{n} v_{ij} z_i (t - \Delta t) + K_0 (t - \Delta t) + K_{1(j)} (t - \Delta t) + K_{2(j)} (t - \Delta t)}, \quad (2)$$

where v_{ij} represents the strength of the synapse from neuron i to neuron j, z_i $(t\text{-}\Delta t)$ has the same meaning as in equation 1, and K_0, $K_{1(j)}$, and $K_{2(j)}$ are inhibition-like terms that will be discussed in more depth later. In this model, neuron j fires if either $y_j(t) >$ ½, or if it receives external forcing input.

2. Necessary Probabilities and Statistics

Mathematically, the necessary forecasting calculation for the idealized CA3 neuron is $P(Z_j(t) = 1 \mid \vec{Z}(t\text{-}\Delta t) = \vec{z})$, where $Z_j(t)$ is the contribution of neuron j to determining whether or not an event is expected to occur, and $\vec{Z}(t\text{-}\Delta t)$ is recurrent input to the CA3. For this to be a forecasting calculation, the event $\vec{Z}(t\text{-}\Delta t) = \vec{z}$ must precede the event $Z_j(t) = 1$. We will use this time ordering of events for the remainder of this discussion, so the implicit term t will be dropped from our equations.

For a single pyramidal neuron in the mammalian CA3, the number of afferent neurons in $\vec{Z}$ is on the order of 10^4, so even if the individual components of $\vec{Z}$ are constrained to be binary, there are $2^{10,000}$ possible values that $\vec{Z}$ can attain. Therefore, most values of $\vec{Z}$ will never be experienced, so $P(Z_j = 1 \mid \vec{Z} = \vec{z})$ will not be calculable simply by examining prior history. However, according to Bayes' Theorem,

$$P\left(Z_j=1 \mid \vec{Z}=\vec{z}\right)=\frac{P\left(\vec{Z}=\vec{z} \mid Z_j=1\right)P\left(Z_j=1\right)}{P\left(Z_j=1\right)P\left(\vec{Z}=\vec{z} \mid Z_j=1\right)+P\left(Z_j=0\right)P\left(\vec{Z}=\vec{z} \mid Z_j=0\right)}, \quad (3)$$

which can be combined with an assumption of approximate conditional independence,

$$P^*\left(\vec{Z}=\vec{z} \mid Z_j=1\right) \approx \prod_{i=1}^{n} P\left(Z_i=z_i \mid Z_j=1\right), \quad (4)$$

where $P^*(\vec{Z}=\vec{z} \mid Z_j=1)$ indicates the approximation that the components of $\vec{Z}$ are independent of one another given the output of neuron j.

The individual probabilities $P(Z_i=z_i \mid Z_j=1)$ can be estimated by the observed average value of Z_i, prior to neuron j firing (that is, prior by Δt) since the values it can take on are only zero and one. Specifically,

$$P\left(Z_i=1 \mid Z_j=1\right)=\overline{Z}_{ij(1)}, \qquad P\left(Z_i=0 \mid Z_j=1\right)=1-\overline{Z}_{ij(1)},$$

$$P\left(Z_i=1 \mid Z_j=0\right)=\overline{Z}_{ij(0)}, \text{ and } \quad P\left(Z_i=0 \mid Z_j=0\right)=1-\overline{Z}_{ij(0)}, \text{ where} \quad (5)$$

$$\overline{Z}_{ij(1)} \overset{def}{=} E\left[Z_i \mid Z_j=1\right] \text{ and } \qquad \overline{Z}_{ij(0)} \overset{def}{=} E\left[Z_i \mid Z_j=0\right]. \quad (6)$$

It is important to note that there is no direct relationship between statistics $\overline{Z}_{ij(0)}$ and $\overline{Z}_{ij(1)}$. Similarly,

$$P\left(Z_j=1\right)=\overline{Z}_j, \text{ where } \qquad \overline{Z}_j \overset{def}{=} E\left[Z_j\right]. \quad (7)$$

Since the z_i terms are binary, the preceding equations can be combined as

$$P^*\left(Z_j=1 \mid \vec{Z}=\vec{z}\right) \approx \frac{\overline{Z}_j \prod_{i=1}^{n} \overline{Z}_{ij(1)}^{z_i}\left(1-\overline{Z}_{ij(1)}\right)^{1-z_i}}{\overline{Z}_j \prod_{i=1}^{n} \overline{Z}_{ij(1)}^{z_i}\left(1-\overline{Z}_{ij(1)}\right)^{1-z_i}+\left(1-\overline{Z}_j\right)\prod_{i=1}^{n} \overline{Z}_{ij(0)}^{z_i}\left(1-\overline{Z}_{ij(0)}\right)^{1-z_i}}. \quad (8)$$

3. McCulloch-Pitts Neuron

At this point equation 8 has some superficial similarities to McCulloch-Pitts neurons, but uses products instead of summation. However, logarithmic manipulation allows equation 8 to be rewritten in a form that conforms more closely to models of the CA3 region based on McCulloch-Pitts neurons. First of all, dividing by the numerator yields

$$P^*\left(Z_j = 1 \middle| \vec{Z} = \vec{z}\right) \approx \left[1 + \frac{\left(1 - \overline{Z}_j\right)}{\overline{Z}_j} \prod_{i=1}^{n} \left(\frac{1 - \overline{Z}_{ij(0)}}{1 - \overline{Z}_{ij(1)}}\right) \left(\frac{\overline{Z}_{ij(0)}\left(1 - \overline{Z}_{ij(1)}\right)}{\overline{Z}_{ij(1)}\left(1 - \overline{Z}_{ij(0)}\right)}\right)^{z_i} \right]^{-1} . \quad (9)$$

Examining the odds instead of the probability further simplifies equation 9 to

$$\frac{P^*\left(Z_j = 1 \middle| \vec{Z} = \vec{z}\right)}{P^*\left(Z_j = 0 \middle| \vec{Z} = \vec{z}\right)} \approx \frac{\overline{Z}_j}{\left(1 - \overline{Z}_j\right)} \prod_{i=1}^{n} \left(\frac{1 - \overline{Z}_{ij(1)}}{1 - \overline{Z}_{ij(0)}}\right) \left(\frac{\overline{Z}_{ij(1)}\left(1 - \overline{Z}_{ij(0)}\right)}{\overline{Z}_{ij(0)}\left(1 - \overline{Z}_{ij(1)}\right)}\right)^{z_i} . \quad (10)$$

To satisfy its role of calculating conditional probability, the neuron fires if the odds exceed some threshold (φ), where $\varphi = 1$ is a logical choice, but not a mandatory choice. This requirement can be written as

$$\frac{\overline{Z}_j}{\left(1 - \overline{Z}_j\right)} \prod_{i=1}^{n} \left(\frac{1 - \overline{Z}_{ij(1)}}{1 - \overline{Z}_{ij(0)}}\right) \left(\overline{Z}_{ij(1)}\left(1 - \overline{Z}_{ij(0)}\right) \middle/ \overline{Z}_{ij(0)}\left(1 - \overline{Z}_{ij(1)}\right)\right)^{z_i} > \phi \quad (11)$$

Taking the natural log of both sides of equation 11 and using the substitutions

$$v_{ij} \overset{def}{=} \ln\left[\overline{Z}_{ij(1)}\left(1 - \overline{Z}_{ij(0)}\right) \middle/ \overline{Z}_{ij(0)}\left(1 - \overline{Z}_{ij(1)}\right) \right], \qquad\qquad K_0 \overset{def}{=} \ln \phi ,$$

$$K_{1(j)} \overset{def}{=} \ln\left(1 - \overline{Z}_j \middle/ \overline{Z}_j\right), \text{ and} \qquad\qquad K_{2(j)} \overset{def}{=} \sum_{i=1}^{n} \ln\left(1 - \overline{Z}_{ij(0)} \middle/ 1 - \overline{Z}_{ij(1)}\right),$$

simplifies equation 11 to

$$\sum_{i=1}^{n} v_{ij} z_i > K_0 + K_{1(j)} + K_{2(j)}.$$ (12)

Equation 12 can be rewritten as

$$2\sum_{i=1}^{n} v_{ij} z_i > \sum_{i=1}^{n} v_{ij} z_i + K_0 + K_{1(j)} + K_{2(j)}, \text{ or}$$

$$y_j(t) \overset{def}{=} \frac{\sum_{i=1}^{n} v_{ij} z_i (t - \Delta t)}{\sum_{i=1}^{n} v_{ij} z_i (t - \Delta t) + K_0 (t - \Delta t) + K_{1(j)} (t - \Delta t) + K_{2(j)} (t - \Delta t)} > \frac{1}{2},$$ (13)

where the explicit dependence on time has been reintroduced for clarity. Equation 13 now fits many models that use McCulloch-Pitts neurons [2, 4], with a threshold fixed at one-half.

4. Biological Interpretation

Therefore, the only information required for a neuron to create reasonable forecasts of the future are the state of its afferent neurons ($z_i(t - \Delta t)$, transmitted through synapses), the expectation of the neuron itself firing ($\bar{Z}_j$) in a computational interval, the expectation of its afferent neurons firing when the neuron fires ($\bar{Z}_{ij(1)}$), and the expectation of its afferent neurons firing when the neuron is quiescent ($\bar{Z}_{ij(0)}$). Mechanisms exist for the neuron to generate approximations for each piece of necessary information.

A neuron's postsynaptic excitability encodes the expectation of its own firing. That is, lower expectation of firing leads to lower excitability. This naturally arises out of the role that $K_{1(j)}$ plays in equation 13. Specifically, decreasing the value of $\bar{Z}_j$ increases the value of $K_{1(j)}$, which decreases the value of y_j.

The expectation of an afferent neuron recently firing given that this neuron is firing ($\overline{Z}_{ij(1)}$) is the statistical correlate of the post-synaptic modification rule described in Levy (1996) [2] and elsewhere. This post-synaptic modification rule only modifies the synaptic weights when the post-synaptic neuron (Z_j) fires. When the post-synaptic neuron fires, the weight is strengthened if the pre-synaptic (afferent) neuron fired in the preceding interval, and weakened if the pre-synaptic neuron was quiescent. Furthermore, Levy, Colbert, and Desmond (1990) [4], demonstrate that the modification rule

$$w_{ij}^{+}\left(t+\Delta t\right)=w_{ij}^{+}\left(t\right)+\mu z_{j}\left(t\right)\left(z_{i}\left(t-\Delta t\right)-w_{ij}^{+}\left(t\right)\right) \tag{14}$$

under assumptions of stationarity and ergodicity leads to $w_{ij}^{+}\rightarrow\overline{Z}_{ij(1)}$ as $t\rightarrow\infty$.

Similarly, the expectation of an afferent neuron recently firing when this neuron is quiescent ($\overline{Z}_{ij(0)}$) is the equivalent of habituation. The synapse becomes habituated to afferent input if it is not followed by a post-synaptic spike, and this habituation decays in the absence of afferent input [4]. The synaptic modification equation of this habituation-like process is

$$w_{ij}^{-}\left(t+\Delta t\right)=w_{ij}^{-}\left(t\right)+\mu\left(1-z_{j}\left(t\right)\right)\left(z_{i}\left(t-\Delta t\right)-w_{ij}^{-}\left(t\right)\right) \tag{15}$$

which leads to $w_{ij}^{-}\rightarrow\overline{Z}_{ij(0)}$ under the same assumptions as those made for equation 14.

Equations 14 and 15 are only valid where synapses exist – weights whose value are zero are not allowed to change in this model. Allowing synaptogenesis in this type of model requires additional consideration.

5. Discussion

Comparing equation 1 to equation 2 requires a comparison of the summation terms that appear in each numerator. These summations are clearly similar with respect to their use of the afferent input information, but there remains a significant difference in the weights attributed to this input. For example, the w_{ij} terms are limited to the range [0,1], but the v_{ij} terms in equation 2 are theoretically unbounded. Rules governing the shedding of ineffectual input discussed by Levy (2004) [3] will limit v_{ij} to be positive, but there is no upper bound to its size. (However, the biological implementation would necessarily have an upper bound.) Additionally, the v_{ij} terms incorporate habituation effects, but the w_{ij} terms do not. Furthermore, the divisive inhibition terms in equations 1 and 2 show more differences than they do similarities. For example, equation 2 has no dependence in these terms on recurrent (feedback) or external (feedforward) input. Conversely, the inhibition terms in equation 1 are constants, although there are variants of equation 1 that effectively allow K_{FB} to dynamically adapt.

A real problem in the conditional probability model is that firing dynamics governed by equations 2, 14, and 15 are unstable. Specifically, neurons that fire more than other neurons will have smaller values of $K_{I(j)}$, which will make them more likely to fire in the future. As a system, this instability is increased, since if the activity of the system as a whole were to increase, the $K_{I(j)}$ and $K_{I(j)}$ terms would decrease while the v_{ij} terms would increase. These changes would in turn cause the activity to increase even more. Inhibitory neurons are one mechanism that could be added to this model to control these activity fluctuations. These inhibitory

interneurons could interact with the pyramidal neurons by adjusting the K_0 term in the denominator. The simplest method would be to increase the odds threshold φ (which alters K_0) if activity is too high, or to decrease it if activity is too low.

The main advantage of the conditional probability model is that it gives insight into the possible functionality of the CA3 neuron as a conditional probability generator for sequence prediction. However, this model can be improved with respect to its biological plausibility. Only a flavor of the underlying biology is given here and interested readers are directed to [4] for a more rigorous treatment.

Acknowledgments

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Ashlie B. Hocking earned a BS in Physics from Georgia Tech, an MS in Physics/Astronomy from Georgia State and a Masters in Computer Science from the University of Virginia and is currently pursuing his PhD in Computer Science from the University of Virginia. His research is performed under the guidance of William B Levy in the Laboratory of Systems Neurodynamics.

William B Levy earned a BA in Psychology from Princeton and a PhD in Psychobiology from the University of California Irvine. He was a Psychology professor at the University of California Riverside from 1974 until 1979 at which point he joined the faculty at the University of Virginia, where he is currently a professor in the Neurological Surgery department and in the Psychology department.