THE UNIVERSITY OF CHICAGO

STOCHASTIC COMPUTATION IN RECURRENT NETWORKS OF SPIKING NEURONS

A THESIS SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE PHYSICAL AND BIOLOGICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF
MASTER OF SCIENCE

GRADUATE PROGRAM IN BIOPHYSICS

BY
CLAYTON W. SEITZ

CHICAGO, ILLINOIS
WINTER 2021

Epigraph

TABLE OF CONTENTS

ACKNOWLEDGMENTS

ABSTRACT

The primate cerebral cortex is a complex system estimated to harbor more than 25 billion neurons communicating via action potentials or 'spikes' and is responsible for many higher-order brain functions including memory and learning. Recent years have hosted many efforts to understand how such complex phenomena emerge from the communication of individual cells. Many studies have provided evidence that long term plasticity (LTP) in synapses permits a long-lasting alteration of network dynamics and, in turn, forms the basis of long-term memory and learning. However, understanding memory formation and learning in the brain is made difficult by the variability in the response of cortical neurons to stimuli. Therefore, capturing the apparent stochastic features of neural activity in computer based models, such as recurrent spiking neural networks (RSNNs), while explaining their manipulation of information mathematically has become the gold standard for computational neuroscience. Models of neural networks derived from statistical mechanics, such as those which assert that the membrane potential of a cortical neuron obeys a form of Langevin dynamics, can potentially account for stochastic network activity. Such models also provide the intriguing interpretation that neural activity represents sampling from a probability distribution - a technique central to statistical inference. Here, we apply a similiar mathematical treatment to the study of an RSNN by modeling the membrane potential statistics of an integrate and fire neuron using Fokker-Planck equations. With this statistical framework in hand, we can recast a network of neurons as a stochastic process in higher dimensions and explore the relationships between synaptic connectivity and its plasticity to the correlation structure of neural spike trains. This approach is also amenable to information theoretic analysis and is a step toward a mathematical relationship between neuroplasticity mechanisms and the emergent computational capabilities of cortical microcircuits.

CHAPTER 1

INTRODUCTION

The quantitative discussion of the dynamics of many complex systems (systems where the number of interacting units N is large) in nature from networks of spiking neurons, geophysical systems, to excitable media, all necessarily require a statistical description. Indeed, enumerating the available states to such a system itself has proven intractable, even for small systems over short time scales. As an example, consider the states of an interacting system of N binary variables denoted $\{z_i\}_{i=1}^{N}$ which might be physically realized as an ensemble of spins in a ferromagnet. Even for extremely small cases such as $N = 100$ the system can take on $2^{100} = 1.26 \times 10^{30}$ different configurations and by $N = 300$ the number of configurations exceed our best estimates for the number of atoms in the known universe. At the same time, we cannot hope to make enough measurements of such a system to estimate the probability distribution over the space of states and make inferences on the organization and interactions of the individual elements based on such a distribution. We can, however, develop model distributions over the available states based on stochastic interaction between the individual units that account for the degrees of freedom which we cannot approach analytically - a technique often employed in the description of the statistical physics of particles. This family of techniques, often formally referred to as Langevin dynamics, is defined by the use of stochastic differential equations to model the evolution of systems with high degrees of freedom. A Fokker-Planck equation allows us to solve for the time evolution of the probability distribution over such a variable, providing insights into the dynamics which cannot be seen from any one trajectory through the space of states.

1.0.1 Models of action potential generation in cortical neurons

The dominating information processing unit in neocortex is the spiking neuron - a neural cell which exhibits transient depolarization of the cell membrane called *spikes*. The membrane

voltage is regulated by a diverse set of highly specific ion channels embedded in the plasma membrane which open and close based on environmental factors such as the membrane potential itself or changes in the concentration of neurotransmitters. This dependence of the so-called *open probability* of ion channels results in changes of the membrane conductance for the ions they transport and is the origin of the non-linear properties of cells in the nervous system. Several mathematical models have been proposed to explain this process in various levels of detail, generally depending on their application. Some consider the biophysical details of action potential generation by considering specific types of ion channels and their dynamics while others neglect such details for the sake of mathematical simplicity. At the same time, models are often classified as conductance-based or current-based, depending on whether they model the membrane conductance explicitly or summarize membrane depolarization as a sum of membrane currents. The famous Hodgkin-Huxley (HH) model published in 1952 was originally used to fit experimental voltage traces measured in the squid giant axon and is arguably the most biophysically accurate of model of membrane depolarization. The membrane potential of an HH neuron evolves according to a a set of ordinary differential equations that include a term for each of the ion channels thought to be critical for the generation of an action potential. In the following paragraphs, we will briefly introduce the Hodgkin-Huxley model alongside an integrate and fire (IF) model to provide context for the following chapters.

Assuming that we can predict the total membrane current of type n deterministically, we can write a generalized differential equation describing the voltage dynamics of a neuron

$$C_m \frac{dV}{dt} = F(V) + \xi(t) \tag{1.1}$$

where we have used a shorthand $\xi(t) = A \sum_n I_n(t)$, I_n is the membrane current per unit area and F is an arbitrary function of the membrane potential and the source of non-linearity.

For the Hodgkin-Huxley model, we have

$$\begin{aligned} F(V) &= -g_L(V)(V - E_L) + g_K(V)(V - E_K) + g_{Na}(V)(V - E_{Na}) \\ &= -g_L(V - E_L) + g_K n^4 (V - E_K) + g_{Na} m^3 h (V - E_{Na}) \end{aligned}$$

and $\xi(t) = I_{inj}(t)$ (an injected stimulus current). Note the additional variables m, n, h which are *gating variables* defining the open probability for their respective channel. To capture the voltage dependence of the channels, they obey their own ODEs

$$\begin{aligned} \frac{dn}{dt} &= \alpha_n(V)(1 - n) - \beta_n(V)n \\ \frac{dm}{dt} &= \alpha_m(V)(1 - m) - \beta_m(V)m \\ \frac{dh}{dt} &= \alpha_h(V)(1 - h) - \beta_h(V)h \end{aligned}$$

where $\alpha(V)$ and $\beta(V)$ are functions of the voltage derived from empirical data. On the other hand, with a leaky integrate and fire model, we simplify and absorb all membrane currents besides the leak into the variable $\xi(t)$ and are left with

$$F(V) = -g_L(V - E_L)$$

which requires that V decays back to a resting value E exponentially with time constant τ, ignoring the explicit dependence of the membrane current on individual voltage-gated channels.

1

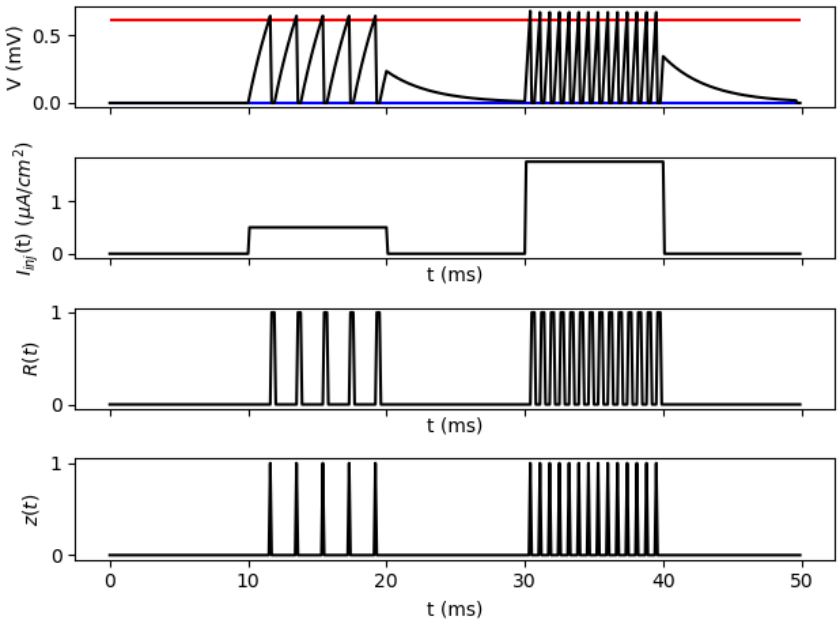


Figure 1.1: Simulation of a leaky integrate and fire neuron

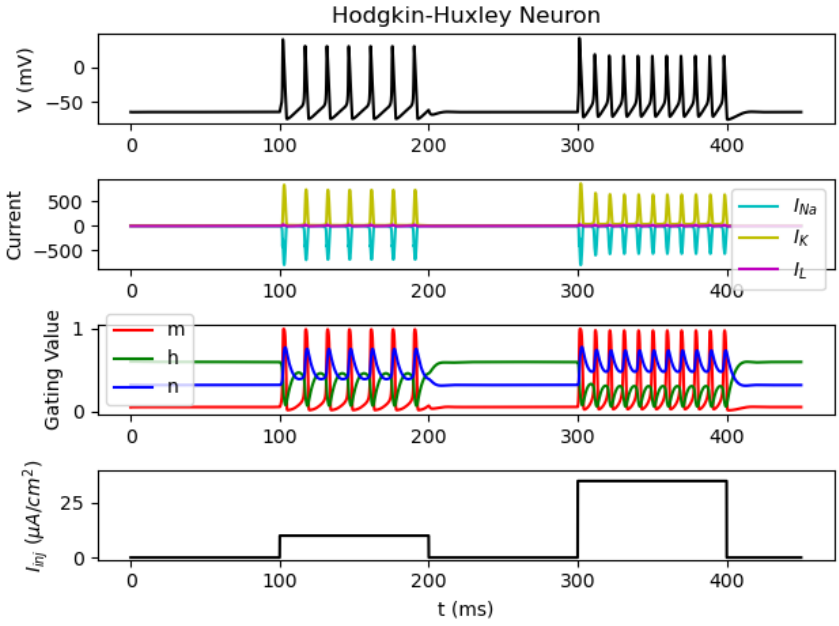


Figure 1.2: Simulation of a Hodgkin-Huxley neuron

1.0.2 Physical models of networks of neurons

Towards the Hopfield network [2] which spawned an entire field of research applying techniques from the statistical physics of spin glasses to the description of neural activity. A popular approach towards the end of 20th century simplified a network of neurons firing action potentials to an ensemble of coupled spins obeying an energy function over the space of states. , the Hopfield model related the patterns learned by a network to the energy landscape over the discrete space of states. The storage capacity of these networks and the geometry of this energy landscape were of particular interest and rigorous mathematical treatment has been used to show limits on the basins of attraction in such energy landscapes [4,10,11].

1.0.3 Origins of stochastic membrane potential dynamics

One of the most prominent conceptual barriers in neuroscience is related to how the brain performs reliable computations with relatively unreliable units. Various patch clamp experiments have shown that neurons tend to fire action potentials in an irregular fashion, even when stimulated with a highly regulated current. This observation has provoked a large numer of studies, many of which have concluded that this irregularity owes its origins to the unreliable transmission of synaptic vesicles. At the same time, stochasticity in the brain along with the reliability of sensory percepts suggest that the brain has evolved around the issue. Indeed, it is possible that this stochasticity is central to the computational paradigm used in cortex. There is, in principle, a very powerful framework for stochastic computation based on sampling from a probability distribution.

Interestingly, an extension of the Hopfield model called the Boltzmann machine actually leverages stochastic activity of Ising spins to perform powerful computations [14]. In such a model, the set of synaptic weights Φ "embody" the joint distribution $P_\Phi(X, R) = P_\Phi(X)P_\Phi(R|X)$ over network inputs and network response, respectively. Then, computa-

tions can be viewed as probabilistic inference after suitable transformations of the weights $\Delta\Phi$. Such physically inspired models have proven useful; however, more recent studies appear have described network dynamics by using Fokker-Planck equations to compute distributions of the membrane voltage as a function of time [5]. Here, we apply a similar formalism to the description of network dynamics with heterogeneous and stochastic synaptic weights to probe the distribution over network states $P_\Phi(R)$ and describe how this framework can be used to provide insights on how the neural networks embody the distribution $P_\Phi(R|X)$ in statistical inference tasks.

1.0.4 The Ornstein-Uhlenbeck Prototype

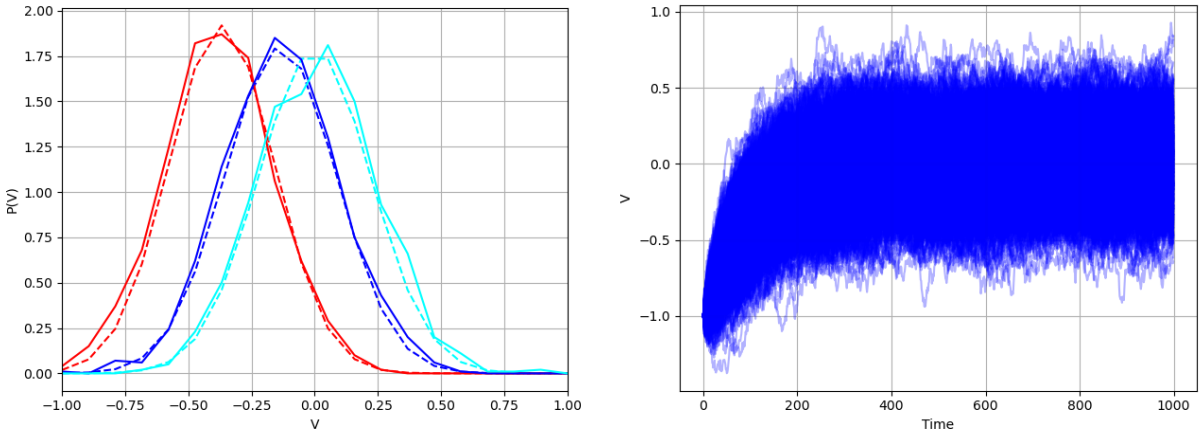
The Ornstein-Uhlenbeck can be thought of as an extension of the Wiener process or *Brownian Motion* where the displacement of a variable x in a time dt is normally distributed with variance proportional to Δt i.e. $x(t+dt) - x(t) \sim N(0, \sigma^2 dt)$ or equivalently $dx \sim \sigma\sqrt{dt}\eta(t)$ where the parameter σ^2 defines the proportionality. The Ornstein-Uhlenbeck process is commonly written as a Langevin equation with a noise term similar to Brownian motion but with an added frictional term $-\theta x(t)$ and non-stationary noise $\mu(t) + \sigma\sqrt{dt}\eta(t)$ giving

$$\dot{x}(t) = -\theta x(t) + \mu(t) + \sigma\sqrt{dt}\eta(t)$$

which, with a simple change of variables, becomes a leaky integrate and fire neuron model for a neuron j

$$\dot{V_j}(t) = -\frac{V_j(t)}{\tau} + \mu_j(t) + \sigma_j\sqrt{dt}\eta(t)$$

we define $I_j(t) = \mu_j(t) + \sigma_j\sqrt{dt}\eta(t)$ as the input current arriving at the soma of a neuron and $\eta(t) \sim \mathcal{N}(0,1)$. To illustrate the applicability of (2.10) in predicting the distribution $P(V,t)$, we consider the case where $\eta(t)$ is a 1D Gaussian white noise. We have the following



(a) (b)

Figure 1.3: Results of numerical integration of a Langevin equation for a gaussian white noise process with $\sigma = 1$, $\Delta t = 0.002$, $\alpha = 10$, and $V(0) = -1$. (a) Distribution of V for $N = 10,000$ units as a function of time (dashed is the theoretical prediction, solid is the simulation result). See stationary distribution in cyan (b) Time course for $N = 10,000$ units

Fokker-Planck equation

$$\tau \dot{P}(V,t) = \frac{\partial}{\partial V}[(V(t) - \mu(t))\, P(V,t)] + \frac{\sigma^2}{2}\frac{\partial^2}{\partial V^2}[P(V,t)] \tag{1.2}$$

The transition density $T(V', t'|V, t)$ has a known analytical form:

$$T(V', t + \Delta t|V, t) = \sqrt{\frac{1}{\tau\pi\sigma^2(1 - \exp\left(-2\Delta t/\tau\right))}} \exp\left(-\frac{1}{\tau\sigma^2}\frac{(V' - V_R \exp(-\Delta t/\tau))^2}{1 - \exp\left(-2\Delta t/\tau\right)}\right)$$

This is equivalent to the distribution $P(V,t)$ as can be seen by plugging T into (2.1) and setting the initial condition $P(V,t) = \delta(V - V_R)$.

CHAPTER 2

THE BRUNEL NETWORK

The moments $M_n(t)$ derived above in the Kramers-Moyal expansion are dependent on the connectivity of the network and the statistics of the input. We will first consider a classic case, where we have a sparse directed network with constant synaptic efficacy between all presynaptic and postsynaptic pairs of cells. This primary pool of neurons is subject to stimulation by N_{in} input neurons with a connection probability γ_{in} giving $C_{\text{in}} = \gamma_{\text{in}} N_{\text{rec}}$ unique connections between the input population and a single neuron in the recurrent pool. Within the recurrent pool, we have a connection probability of $\gamma_{\text{rec}} << 1$ for any pair giving $C_{\text{rec}} = \gamma_{\text{rec}} N_{\text{rec}}$ recurrent inputs per postsynaptic cell. We assume that a presynaptic action potential invokes a post synaptic potential (PSP) with magnitude J_0 in the postsynaptic cell with $J_0 << \theta$ for both input and recurrent projections. The first moment of the transition operator $T(V', t|V, t-\tau)$ is given by

$$\begin{aligned}
\mu(t) &= \mu_{in} + \mu_{rec}(t) \\
&= \left(C_{\text{in}}\nu_{\text{in}}(t) + C_{\text{rec}}\nu_{\text{rec}}(t)\right)\tau\langle J\rangle \\
&= \left(C_{\text{in}}\nu_{\text{in}}(t) + C_{\text{rec}}\nu_{\text{rec}}(t)\right)\tau J_0
\end{aligned}$$

where $\nu_{\text{in}}(t)$ is the rate parameter for the input Poisson process. The second moment

$$\begin{aligned}
\sigma^2(t) &= \sigma^2_{\text{rec}} + \sigma^2_{\text{ext}} \\
&= \left(C_{\text{in}}\nu_{\text{in}}(t) + C_{\text{rec}}\nu_{\text{rec}}(t)\right)\tau\langle J^2\rangle \\
&= \left(C_{\text{in}}\nu_{\text{in}}(t) + C_{\text{rec}}\nu_{\text{rec}}(t)\right)\tau J_0^2
\end{aligned}$$

After inserting the first two moments into (2.10) we arrive at the following Fokker-Planck equation

$$\dot{P}(V,t) = -\frac{\partial}{\partial V}[\mu(t)P(V,t)] + \frac{1}{2}\frac{\partial^2}{\partial V^2}[\sigma^2(t)P(V,t)]$$

At this point, it is necessary to impose the appropriate boundary conditions on the above Fokker-Planck equation as in so as to maintain biological realism. The Fokker-Planck equation can be written as the continuity equation

$$\frac{\partial P(v,t)}{\partial t} = -\frac{\partial S}{\partial V}$$

(Risken, 1984) with

$$S(V,t) = -\frac{v - V_L - \mu}{\tau}P(V,t) - \frac{\sigma^2(t)}{2\tau}\frac{\partial P(V,t)}{\partial V}$$

which is known as the *probability current* through voltage V at a time t. The instantaneous firing rate is equivalent to the probability current through the threshold i.e. $\nu(t) = S(\theta,t)$. Furthermore, we require that the probability current through the firing threshold $P(\theta,t) = 0$ and that instead this probability emerges at the resting potential after a refactory period of τ_{ref}. This condition gives the following boundary condition for the derivative of the probability with respect to voltage

$$\frac{\partial P(\theta,t)}{\partial V} = -\frac{2\tau\nu(t)}{\sigma^2(t)}$$

To account for the refractory period τ_{ref}, we define an auxililary distribution

$$p_r(t) = \int_{t-\tau_{\text{ref}}}^{t} \nu(t)dt$$

which together with the distribution $P(V,t)$ satisfy the normalization condition:

$$\int P(v,t)dV + p_r(t) = 1$$

$$\frac{\partial P(v,t)}{\partial t} = \left(\mu(t) - \frac{v - v_L}{\tau}\right)\frac{\partial}{\partial v}P(v,t) - \frac{\sigma^2(t)}{2\tau}\frac{\partial^2}{\partial v^2}P(v,t) + \nu(t-\tau_{\text{ref}})\delta(v - V_R)$$

which we approximate by central finite differences

$$\begin{aligned}\frac{p(v,t+\Delta t) - p(v,t)}{\Delta t} = &\left(\mu(t) - \frac{v - v_L}{\tau} + \mu_{ext}\right)\frac{p(v+\Delta v,t) - p(v,t)}{\Delta v} \\ &- \frac{1}{2}\left(\sigma^2(t) + \sigma^2_{ext}\right)\frac{p(v+\Delta v,t) - 2p(v,t) + p(v-\Delta v,t)}{\Delta v^2}\end{aligned}$$

We consider a general network of N leaky integrate and fire units expressed mathematically as a weighted graph $\mathcal{N}$. We defined the state vector $\mathbf{V}$ that stores the membrane potential of each cell, which evolves according to a set of N coupled differential equations

$$\dot{V}_j(t) = -\frac{V_j(t)}{\tau} + \sum_i J_{ij}\delta(t - t_{spike}) + X_j(t)$$

for a stochastic input X, which we assume can be written as a compound Poisson process, and a weighted summation of spikes in the primary population $\sum_i J_{ij}\delta(t - t_{spike})$. The state vector for the system is then $\mathbf{V}(t) = (V_0(t), V_1(t), ..., V_N(t))$ and we look for an analytical

relationship between the joint distribution $P(\mathbf{V}(t))$ and the synaptic connectivity J. In principle, if we know the moments $\{M_j^n\}$ of the transition operator $T_j(V', t'|V, t)$ for every neuron j to arbitrary order, we can express $\dot{P}(\mathbf{V}(t))$ according to the KM expansion in (2.7). The primary hurdle we need to overcome in this procedure then becomes relating the moments $\{M_j^n\}$ to the synaptic connectivity J. For example, we can construct a general template for the distribution T_j by noticing that the probability of a binary input pattern

$$P(\mathbf{z}) = \prod_j p_j^{z_j}(1-p_j)^{1-z_j}$$

which is a multivariate Bernoulli distribution. If we let ξ index the space of possible binary patterns

$$T(V', t'|V, t) = \sum_\xi \delta(V' - V - J \cdot z_\xi) \prod_j p_j^{z_j}(1-p_j)^{1-z_j} \tag{2.1}$$

so we see that we must first know $P(\mathbf{z})$ which in turn requires knowledge of all $p_j = P_j(\theta, t)$ i.e. the probability flux at the threshold θ. We now argue that the moments of (2.8) can be found

$$M_n = \int (V - V')^n T(V', t'|V, t) dV \tag{2.2}$$

which are essentially the moments of a compound Bernoulli distribution where the individual probabilities $p_j(t')$ are given by $P_j(\theta, t)$.

Appendices

APPENDIX A

THE KRAMERS-MOYAL EXPANSION

Given many instantiations of a stochastic variable V, we can construct a normalize histogram over all observations as a function of time $P(V,t)$. However, in order to systematically explore the relationship between the parameterization of the process and $P(V,t)$ we require an expression for $\dot{P}(V,t)$. If we make a fundamental assumption that the evolution of $P(V,t)$ follows a Markov process i.e. its evolution has the memoryless property, then we can write

$$P(V',t) = \int T(V',t|V,t-\tau)P(V,t-\tau)dV \tag{A.1}$$

which is known at the Chapman-Kolmogorov equation. The factor $T(V',t|V,t-\tau)$ is known as the *transition operator* in a Markov process and determines the evolution of $P(V,t)$ in time. We proceed by writing $T(V',t|V,t-\tau)$ in a form referred to as the Kramers-Moyal expansion

$$\begin{aligned} T(V',t|V,t-\tau) &= \int \delta(u-V')T(u,t|V,t-\tau)du \\ &= \int \delta(V+u-V'-V)T(u,t|V,t-\tau)du \end{aligned}$$

If we use the Taylor expansion of the δ-function

$$\delta(V+u-V'-V) = \sum_{n=0}^{\infty} \frac{(u-V)^n}{n!}\left(-\frac{\partial}{\partial V}\right)^n \delta(V-V')$$

Inserting this into the result from above, pulling out terms independent of u and swapping the order of the sum and integration gives

$$T(V', t|V, t-\tau) = \sum_{n=0}^{\infty} \frac{1}{n!} \left(-\frac{\partial}{\partial V}\right)^n \delta(V - V') \int (u - V)^n T(u, t|V, t-\tau) du \tag{A.2}$$

$$= \sum_{n=0}^{\infty} \frac{1}{n!} \left(-\frac{\partial}{\partial V}\right)^n \delta(V - V') M_n(V, t) \tag{A.3}$$

noticing that $M_n(V,t) = \int (u-V)^n T(u,t|V,t-\tau)du$ is just the nth moment of the transition operator T. Plugging (2.6) back in to (2.4) gives

$$P(V,t) = \int \left(1 + \sum_{n=1}^{\infty} \frac{1}{n!} \left(-\frac{\partial}{\partial V}\right)^n M_n(V,t)\right) \delta(V - V') P(V, t-\tau) dV \tag{A.4}$$

$$= P(V', t-\tau) + \sum_{n=1}^{\infty} \frac{1}{n!} \left(-\frac{\partial}{\partial V}\right)^n [M_n(V,t) P(V,t)] \tag{A.5}$$

Approximating the derivative as a finite difference and taking the limit $\tau \to 0$ gives

$$\dot{P}(V,t) = \lim_{\tau \to 0} \left(\frac{P(V,t) - P(V, t-\tau)}{\tau}\right) \tag{A.6}$$

$$= \sum_{n=1}^{\infty} \frac{1}{n!} \left(-\frac{\partial}{\partial V}\right)^n [M_n(V,t) P(V,t)] \tag{A.7}$$

which is formally known as the Kramers-Moyal (KM) expansion. The Fokker-Planck equation is a special case of (2.10) where we neglect terms $n > 2$ in the *diffusion approximation*.

[1] Mculloch and Pitts. *A logical calculus of the ideas imminent in nervous activity.* Journal of Mathematical Biophysics. 1943.

[2] J.J. Hopfield. *Neural networks and physical systems with emergent collective computational abilities.* 1982.

[3] D.J. Amit. *Spin-glass models of neural networks.* Physical Rev A. 1985.

[4] E. Gardner. *The space of interactions in neural network models.* Journal of Physics A: Mathematical and General. 1988.

[5] N. Brunel. *Dynamics of sparsely connected networks of excitatory and inhibitory neurons.* Journal of Computational Neuroscience. 2000.

[6] Rosenbaum and Doiron. *Balanced Networks of Spiking Neurons with Spatially Dependent Recurrent Connections.* Physical Review X. 2014.

[7] Zenke et al. *Diverse synaptic plasticity mechanisms orchestrated to form and retrieve memories in spiking neural networks.* Nature Communications. 2015.

[8] Williams et al. *Nonnegative decomposition of multivariate information.* arXiv. 2010.

[9] Amit et al. *Storing infinite numbers of patterns in a spin-glass model of neural networks.* Physical Rev. Letters. 1985

[10] Nishimori. *Statistical physics of spin glasses and information processing: an introduction.* Clarendon Press. 2010

[11] Buesing et al. *Neural Dynamics as Sampling: A Model for Stochastic Computation in Recurrent Networks of Spiking Neurons.* PLOS Computational Biology. 2011

[12] Pecevski et al. *Learning Probabilisitc Inference through Spike-Timing-Dependent Plasticitys.* eNeuro. 2016

[13] Pecevski et al. *Formation and maintenance of neuronal assemblies through synaptic plasticity.* Nature Communications. 2014

[14] Pecevski et al. *A learning algorithm for Boltzmann Machines.* Cognitive Science. 1985