Computational Neuroscience: Bibliographic Annotations and Thoughts on Selected Texts

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References

[1] A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve," in *Journal of Physiology, Volume 117*, March 1952.

Possibly one of the most important papers in modern neuroscience (as seen by almost 30,000 citations on Google Scholar), Hodgkin and Huxley use the experimental data they collected from voltage clamp techniques on giant squid axons to attempt to build a quantitative framework for neuronal communication and action potentials. Because theoretical neuroscience was such an infant field in 1952, the beginning of this article postulated ideas for the biological mechanisms of what we now know as an electrochemical process in which a resting membrane potential is built up by transmembrane protein transporters who, with the help of ATP and ionic concentration gradients, actively build a potential of around -75 mV between the inside and outside of a membrane. Some of their ideas included ionic coupling of sodium with some negative sister molecule which served to alter the membrane potential when the time arose for signal propagation. After this, they dove into mathmatical models, seeking to represent data collected quantitatively with systems of equations that best governed communicative processes between neurons. First, they build up rate constants whose form follows that of a Boltzmann distribution function, or C*exp(-E/kT). In place of "E", or energy, they input voltage. One of the conclusions of the models they build up for conductance and rate equations is that the rate that the membrane potential reaction progresses is dependent of the concentration and current variables of ions involved in reactions (primarily sodium and potassium ions) as well as the time variable T. They test this out experimentally, and find out that sure enough, temperature differences induce phase changes of potential curves. Overall, this paper is of paramount importance in theoretical neuroscience. Hodgkin and Huxley used systems of equations to build up models of action potentials and (mostly) sucessfully stacking these models up to experimental findings, where they held firm. In doing so, these neuroscientists paved the way for exploration of both microbiological theory of action potentials and a fundamental understanding of how nerve cells communicate.

[2] W. McCulloch and W. Pitts, "A logical calculus of the ideas immanent in nervous activity." in *The bulletin of mathematical biophysics 5.4*, 1943.

Regarded as a seminal paper in computational neuroscience as well as the basis of modern machine learning, the importance of the early formulations of McCulloch and Pitts are hard to overstate. By treating the biological existence of neurons as computational devices, these scientists applied logical theory to biological systems, most notably coming up with the idea that the communicative signaling of neurons was "all-or-nothing" and could, in theory, be quantified by algorithms that utilized AND, OR, and NOT gates. Excluding the mathematical portion of the model, the dendritic equivalent of this modeled neuron receives one or more input signals. Next, the collection of signals are processed according to weight (excitatory weight and/or inhibitory weight). After this, a binary output is determined, either 0 or 1 with zero representing no firing of the "action potential" and 1 representing firing of the "action potential". Though simplicstic in design, this model of a single neuron was profound in that it allowed for a quantitative basis of the neuron, demystifying the most integral component of the nervous system.

[3] C. Shannon, "A mathematical theory of communication," in *Bell System Technical Journal*, 1948.

Claude Shannon wrote this groundbreaking article to explore the stochastic and statistical dependencies communication. He based the mathematical framework on Markov chains, which are extensions of Bernoulli's statistical formulations to dependent events through a kind of mathematical "memory". Markov postulated that dependent events have a memory of prior event(s) which affects the outcome of the current event. As a result, dependent events also converge to some distribution or function given sufficient data/input. This idea and Shannon's curiosity about human communication set the tone for the creation of his theory.

Shannon first builds up the language needed to tackle english communication and introduce some random sequence of letters (A,B,C) the we will seek to replicate using Markov chain principles. Next, the first model is build up. The first-order condition-dependent algorithm tries to emulate some sequence of letters by essentially weighting probabilities of each component letter so that the frequency of letters in the final sequence will be approximately the same between model and original sequence. To make things better, we can take into account which *pair* of letters are randomly selected and create a condition-dependent algorithm that selects a pair of letters, and the next letter picked will be dependent on the last letter of the previous pair. Now, we have gone from similar frequencies to similar frequencies *and* more similar looking sequences built up between model and original. For simple purposes, this is very good at creating similar-looking sequences and can be expanded upon in a third-order approximation which takes into account groups of three letters. This can continue on as many orders of approximation as computation allows, but at some point the complexity of the computation exceeds the scope of what we are trying to accomplish, so we are satisfied with some order less than too much.

This principle of creating condition-dependent algorithms for sequences of letters can be scaled up to sequences of words, which Shannon does and shows that comprehensible sentences emerge as our model increases in the order of complexity. This is all interesting, but what is most relevant to computational neuroscience is "information entropy" which was defined by Shannon in this same article. Entropy in this context is the expected value of the self-information of a variable. Just like in thermodynamics, the entropy tends to increase as the data grows and in information theory, this means that the more data we have, the more we can know about the dependencies of some events on others.

Learning this bit of information theory has given me access to the understanding of some mathematical models used to emulate sequences and patterns. As put by Timme and Lapish in their 2018 article on information theory in neuroscience: "...data from neuroscience experiments are multivariate, the interactions between the variables are nonlinear, and the landscape of hypothesized or possible interactions between variables is extremely broad. Information theory is well suited to address these types of data, as it possesses multivariate analysis tools, it can be applied to many different types of data, it can capture nonlinear interactions, and it does not require assumptions about the structure of the underlying data..." Therefore, learning from information theory is important in figuring out the best way to process and think about neuronal data.