

10

Conclusion

Recent advances in neural recording technologies have stirred great excitement. It seems that a more complete understanding of neural computation is within our grasp. Armed with these powerful tools, we can peer into the brain and observe the activity of most, if not all, of the neurons in a circuit. What a major advance over the handfuls of neurons we were limited to only a few years ago! All we must do is extract the underlying patterns and principles from these large scale recordings.

While these advances present unprecedented opportunities, the task of translating data into understanding is far from trivial. The human genome has been known for a decade now ([Consortium et al., 2004](#); [Gregory et al., 2006](#)), yet much of its structure remains enigmatic. The connectome of the nematode *C. Elegans* has been known for three decades ([White et al., 1986](#)), yet our understanding of this simple organism with fewer than 400 neurons is still incomplete. At the heart of these endeavors is the search for meaningful abstractions and structured representations given complex and noisy data. Our success in reverse engineering neural computation relies critically on our ability to discover such structure. This thesis has developed a number of methods for instantiating structural hypotheses in the form of probabilistic models and turning the crank of Bayesian inference in order to reason about them.

I believe the path forward lies in the iterative refinement of theories guided by both top-down considerations of algorithmic goals and complexity-theoretic constraints, and bottom-up, data-driven analyses of neural data. The Bayesian methods presented in this thesis are designed to accelerate this process, providing “data microscopes” that allow us to visualize complex, high-dimensional data in new and interpretable ways. I will briefly discuss two directions in which these methods should continue to be developed.

10.1 TOWARD PROGRAMMATIC MODELS OF NEURAL COMPUTATION

As we have shown here, hierarchical probabilistic models provide an intuitive language for capturing different types of abstraction, allowing us to formalize generative processes of how data comes to be. However, as these models grow in scope and scale, the language of probabilistic models becomes cumbersome. At the same time, as our models grow in complexity, they look more and more like *probabilistic programs* (Goodman et al., 2008).

The probabilistic models developed in this thesis can all be written in this way. For example, the hidden Markov models of Chapter 7 are equivalent to the following program:

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Require:  $\pi^{(0)}, P, \Lambda$ 
for  $t = 1, \dots, T$  do
  if  $t = 1$  then
     $z_t \sim \text{Discrete}(\pi^{(0)})$ 
  else
     $z_t \sim \text{Discrete}(\pi^{(z_{t-1})})$ 
  end if
  for  $n = 1, \dots, N$  do
     $s_{t,n} \sim \text{Poisson}(\lambda_{z_t,n})$ 
  end for
end for

```

Program 10.1: Programmatic representation of a hidden Markov model.

This representation is equivalent to the probabilistic model (it implies the same distribution over \mathbf{z} and \mathbf{S}), but this description combines stochastic operations, like sampling, with basic control flow, like **if** statements and **for** loops. This powerful combination not only enables rapid formulation of models for neural data, it also forms the basis for a “probabilistic language of thought,” an idea that is taking hold in cognitive science (Goodman

et al., 2014). As we seek to bridge the gap between cognitive algorithms and neural implementations, it will help if we are speaking the same language.

Of course, the “no free lunch” theorem applies here as well. While probabilistic programming languages make it easy to specify complex generative processes, they make it just as easy to specify models for which Bayesian inference is completely intractable. While much progress has been made in general purpose inference algorithms (Goodman et al., 2008; Ranganath et al., 2014; Mansinghka et al., 2014; Wood et al., 2015; Kucukelbir et al., 2015), these “black box” inference algorithms are, by design, not capitalizing on model-specific structure that the rather bespoke inference algorithms of this thesis have leveraged. This will certainly change as probabilistic program “compilers” become more adept at recognizing model structure, but this is currently a major challenge.

10.2 TOWARD JOINT MODELS OF NEURAL ACTIVITY, BEHAVIOR, AND ENVIRONMENT

This thesis has focused solely on modeling the dynamics and structure of neural spike trains, however, this data is often collected from organisms as they perform natural behaviors in complex behaviors. For example, massive recordings are now being collected from animals in decision making (e.g. Briggman et al., 2005), freely behaving (e.g. Prevedel et al., 2014), and evoked response (e.g. Portugues et al., 2014) tasks. This type of data provides a tremendous opportunity to study the relationship between neural activity, natural behavior, and environment. But first, we must formulate and fit a model that captures both the complex dynamics of neural activity, the rich repertoire of behavior, and the environmental state. The models and inference algorithms designed in this thesis capture core notions of state and dynamics that can be extended, in an intuitive way, to these types of recordings.

For example, large-scale recordings have revealed that ensembles of neurons reliably participate together during natural or trained behavior, suggesting that task-related neural activity might be lower-dimensional than the number of recorded neurons, and that these neurons might evolve through different states over time in an environmentally dependent manner. The dynamical system models developed in this thesis can naturally instantiate these hypotheses. Consider a model in which neural spike trains, \mathbf{s}_t , behavioral time series, \mathbf{b}_t , and environmental stimuli, \mathbf{e}_t , are simultaneously measured. A simple hypothesis is

that the neural spike trains and the behavior are conditionally independent given underlying states, \mathbf{x}_t and \mathbf{z}_t , and that the evolution of these states depends on the environment, \mathbf{e}_t . Such a model enables us to identify the low dimensional states of neural activity and overt behavior, as well as their dynamics. Moreover, it enables us to predict one given the others. With relatively minor adjustments, the inference algorithms developed previously can be extended to handle these multimodal datasets.

Ultimately, the goal of computational and systems neuroscience is to understand this interplay between environment, neural activity, and behavior. As with all scientific endeavors, our success will be measured in our ability to articulate theories of neural computation that explain, in simpler terms, the complex nature of these multifaceted systems. With the advent of recording technologies capable of probing neural circuits at unprecedented scale and advances in machine learning providing the computational and statistical tools for making sense of complex data, it seems the stage is set for major breakthroughs in our understanding of nature's most sophisticated computer: the human brain.

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