
To survive, organisms must extract information from the past that is relevant for their future. How this process is expressed at the neural level remains unclear. We address this problem by developing a novel approach from first principles. We show here how to generate low-complexity representations of the past that produce optimal predictions of future events. We then illustrate this framework by studying the coding of 'oddball' sequences in auditory cortex. We find that for many neurons in primary auditory cortex, trial-by-trial fluctuations of neuronal responses correlate with the theoretical prediction error calculated from the short-term past of the stimulation sequence, under constraints on the complexity of the representation of this past sequence. In some neurons, the effect of prediction error accounted for more than 50% of response variability. Reliable predictions often depended on a representation of the sequence of the last ten or more stimuli, although the representation kept only few details of that sequence.


Previous reinforcement-learning models of the basal ganglia network have highlighted the role of dopamine in encoding the mismatch between prediction and reality. Far less attention has been paid to the computational goals and algorithms of the main-axis (actor). Here, we construct a top-down model of the basal ganglia with emphasis on the role of dopamine as both a reinforcement learning signal and as a pseudo-temperature signal controlling the general level of basal ganglia excitability and motor vigilance of the acting agent. We argue that the basal ganglia endow the thalamic-cortical networks with the optimal dynamic tradeoff between two constraints: minimizing the policy complexity (cost) and maximizing the expected future reward (gain). We show that this multi-dimensional optimization processes results in an experience-modulated version of the softmax behavioral policy. Thus, as in classical softmax behavioral policies, probability of actions are selected according to their estimated values and the pseudo-temperature, but in addition also vary according to the frequency of previous choices of these actions. We conclude that the computational goal of the basal ganglia is not to maximize cumulative (positive and negative) reward. Rather, the basal ganglia aim at optimization of independent gain and cost functions. Unlike previously suggested single-variable maximization processes, this multi-dimensional optimization process leads naturally to a softmax-like behavioral policy. We suggest that beyond its role in the modulation of the efficacy of the cortico-striatal synapses, dopamine directly affects striatal excitability and...
thus provides a pseudo-temperature signal that modulates the tradeoff between gain and cost. The resulting experience and dopamine modulated softmax policy can then serve as a theoretical framework to account for the broad range of behaviors and clinical states governed by the basal ganglia and dopamine systems.

2009


The study of complex information processing systems requires appropriate theoretical tools to help unravel their underlying design principles. Information theory is one such tool, and has been utilized extensively in the study of the neural code. Although much progress has been made in information theoretic methodology, there is still no satisfying answer to the question: "What is the information that a given property of the neural population activity (e.g., the responses of single cells within the population) carries about a set of stimuli?" Here, we answer such questions via the minimum mutual information (MinMI) principle. We quantify the information in any statistical property of the neural response by considering all hypothetical neuronal populations that have the given property and finding the one that contains the minimum information about the stimuli. All systems with higher information values necessarily contain additional information processing mechanisms and, thus, the minimum captures the information related to the given property alone. MinMI may be used to measure information in properties of the neural response, such as that conveyed by responses of small subsets of cells (e.g., singles or pairs) in a large population and cooperative effects between subunits in networks. We show how the framework can be used to study neural coding in large populations and to reveal properties that are not discovered by other information theoretic methods.


Biological systems need to process information in real time and must trade off accuracy of presentation and coding costs. Here we operationalize this trade-off and develop an information-theoretic framework that selectively extracts information of the input past that is predictive about the output future, obtaining a generalized eigenvalue problem. Thereby, we unravel the input history in terms of structural phase transitions corresponding to additional dimensions of a state space. We elucidate the relation to canonical correlation analysis and give a numerical example. Altogether, this work relates information-theoretic optimization to the joint problem of system identification and model reduction.

2008


Several models have suggested that information transmission in the basal ganglia (BG) involves gating mechanisms, where neuronal activity modulates the extent of gate aperture and its duration. Here, we
demonstrate that BG response duration is informative about a highly abstract stimulus feature and show that the duration of "gate opening" can indeed be used for information transmission through the BG. We analyzed recordings from three BG locations: the external part of the globus pallidus (GPe), the substantia nigra pars reticulata (SNr), and dopaminergic neurons from the substantia nigra pars compacta (SNc) during performance of a probabilistic visuomotor task. Most (>85%) of the neurons showed significant rate modulation following the appearance of cues predicting future reward. Trial-to-trial mutual information analysis revealed that response duration encoded reward prospects in many (42%) of the responsive SNr neurons, as well as in the SNc (26.9%), and the GPe (29.3%). Whereas the low-frequency discharge SNc neurons responded with only an increase in firing rate, SNr and GPe neurons with high-frequency tonic discharge responded with both increases and decreases. Conversely, many duration-informative neurons in SNr (68%) and GPe (50%) responded with a decreased rather than an increased rate. The response duration was more informative than the extreme (minimal or maximal) amplitude or spike count in responsive bins of duration-informative neurons. Thus response duration is not simply correlated with the discharge rate and can provide additional information to the target structures of the BG.

2007


The development of bioinformatic tools by individual labs results in the abundance of parallel programs for the same task. For example, identification of binding site regions between interacting proteins is done using: ProMate, WHISCY, PPI-Pred, PINUP and others. All servers first identify unique properties of binding sites and then incorporate them into a predictor. Obviously, the resulting prediction would improve if the most suitable parameters from each of those predictors would be incorporated into one server. However, because of the variation in methods and databases, this is currently not feasible. Here, the protein-binding site prediction server is extended into a general protein-binding sites research tool, ProMateus. This web tool, based on ProMate’s infrastructure enables the easy exploration and incorporation of new features and databases by the user, providing an evaluation of the benefit of individual features and their combination within a set framework. This transforms the individual research into a community exercise, bringing out the best from all users for optimized predictions. The analysis is demonstrated on a database of protein protein and protein-DNA interactions. This approach is basically different from that used in generating meta-servers. The implications of the open-research approach are discussed. ProMateus is available at http://bip.weizmann.ac.il/promate.

2006


Information processing by a sensory system is reflected in the changes in stimulus representation along its successive processing stages. We measured information content and stimulus-induced redundancy in the neural responses to a set of natural sounds in three successive stations of the auditory pathway-inferior colliculus (IC), auditory thalamus (MGB), and primary auditory cortex (A1). Information about stimulus identity was somewhat reduced in single A1 and MGB neurons relative to single IC neurons, when
information is measured using spike counts, latency, or temporal spiking patterns. However, most of this difference was due to differences in firing rates. On the other hand, IC neurons were substantially more redundant than A1 and MGB neurons. IC redundancy was largely related to frequency selectivity. Redundancy reduction may be a generic organization principle of neural systems, allowing for easier readout of the identity of complex stimuli in A1 relative to IC.


The information bottleneck (IB) method is an unsupervised model independent data organization technique. Given a joint distribution, $p(X, Y)$, this method constructs a new variable, $T$, that extracts partitions, or clusters, over the values of $X$ that are informative about $Y$. Algorithms that are motivated by the IB method have already been applied to text classification, gene expression, neural code, and spectral analysis. Here, we introduce a general principled framework for multivariate extensions of the IB method. This allows us to consider multiple systems of data partitions that are interrelated. Our approach utilizes Bayesian networks for specifying the systems of clusters and which information terms should be maintained. We show that this construction provides insights about bottleneck variations and enables us to characterize the solutions of these variations. We also present four different algorithmic approaches that allow us to construct solutions in practice and apply them to several real-world problems.

2004


Stochastic computing has a broad range of applications, yet electronic computers realize its basic step, stochastic choice between alternative computation paths, in a cumbersome way. Biomolecular computers use a different computational paradigm and hence afford novel designs. We constructed a stochastic molecular automaton in which stochastic choice is realized by means of competition between alternative biochemical pathways, and choice probabilities are programmed by the relative molar concentrations of the software molecules coding for the alternatives. Programmable and autonomous stochastic molecular automata have been shown to perform direct analysis of disease-related molecular indicators in vitro and may have the potential to provide in situ medical diagnosis and cure.


A major obstacle in applying various hypothesis testing procedures to datasets in bioinformatics is the computation of ensuing p-values. In this paper, we define a generic branch-and-bound approach to efficient exact p-value computation and enumerate the required conditions for successful application. Explicit procedures are developed for the entire Cressie-Read family of statistics, which includes the widely used Pearson and likelihood ratio statistics in a one-way frequency table goodness-of-fit test. This new formulation constitutes a first practical exact improvement over the exhaustive enumeration performed by existing statistical software. The general techniques we develop to exploit the convexity of many statistics are also shown to carry over to contingency table tests, suggesting that they are readily extendible to other
tests and test statistics of interest. Our empirical results demonstrate a speed-up of orders of magnitude over the exhaustive computation, significantly extending the practical range for performing exact tests. We also show that the relative speed-up gain increases as the null hypothesis becomes sparser, that computation precision increases with increase in speed-up, and that computation time is very moderately affected by the magnitude of the computed p-value. These qualities make our algorithm especially appealing in the regimes of small samples, sparse null distributions, and rare events, compared to the alternative asymptotic approximations and Monte Carlo samplers. We discuss several established bioinformatics applications, where small sample size, small expected counts in one or more categories (sparseness), and very small p-values do occur. Our computational framework could be applied in these, and similar cases, to improve performance.

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