Collin Allen University of Pittsburgh

Reconciling Dynamical and Computational Models

In 1995, Timothy van Gelder used dynamical systems theory to propose an answer to the question "What might cognition be if not computation?" Using intuitions that were pumped by thinking about the Watt governor, he argued that continuous dynamical models are incompatible with computation over discrete representations. I will sketch an argument mounted by Weinberger & Allen (2022) to the effect that a closer look at the static-dynamic hybridity of the cognitive dynamical models reveals features that van Gelder ignored. Combined with a more pragmatist stance towards modeling, this makes his anti-computationalist case weaker. However, since our analysis stems from work on toy systems by Randy Beer, the question remains whether it scales up to neural dynamics in actual brains. I will discuss the prospects for answering this question, using an example from systems neuroscience.

-----Veronica A. Alvarez NIMH

A circuit mechanism for cortical control over striatal dopamine that is targeted by drugs of abuse

The addictive properties of drugs of abuse are driven by the forceful combination of rewarding effects and loss of cognitive inhibitory control over behavior, which often leads to repeated uncontrollable drug consumption. The mechanism underlying the rewarding effects are fairly understood and involve elevation of striatal dopamine in response to activation of midbrain dopamine neurons. The mechanisms underlying the loss of cognitive control over behavior are less understood and thought to involve activation of medial prefrontal cortex (mPFC) and their subcortical projections.

The data presented showed that activation of mPFC projections to the striatum can evoke striatal dopamine signals in vivo. These cortical-evoked dopamine signals are generated locally within the striatum through the recruitment of striatal cholinergic interneurons, resulting in dopamine release that is independent of the somatic activation of midbrain dopamine neurons. With the right timing, activation of the mPFC projections can suppress the magnitude of dopamine signals evoked by midbrain dopamine neurons, thus providing a multi-synaptic mechanism for cortical control over striatal dopamine. When these mPFC projections are engaged, a brief pause in firing of the cholinergic interneurons can enhance striatal dopamine signals by lessening the suppression.

Surprisingly, all drugs of abuse tested inhibited cortical-evoked dopamine resulting in a boosting of the dopamine signals evoked by midbrain neuron stimulation, classically associated with reward. We propose that the suppression of cortical-evoked dopamine confers drugs of abuse with the ability to impair cognitive inhibitory control over striatal dopamine and enhance reward related dopamine signals, ultimately leading to repeated uncontrollable drug consumption. The study provides important insights into the mechanisms underlying the addictive properties of drugs of abuse and has implications for the development of potential treatments for addiction.

Bruno Averbeck NIMH

Synaptic pruning and developmental neurodynamics

Adolescent development is characterized by an improvement in multiple cognitive processes. While performance on cognitive operations improves during this period, the ability to learn new skills quickly, for example a new language, decreases. During this time there is substantial pruning of excitatory synapses in cortex, and specifically in prefrontal cortex. We examined the effects of synaptic pruning using recurrent network models trained to carry out cognitive tasks, similar to those on which adolescents improve. We found that the pruning led to improved efficiency in the networks. Additionally, the pruning led to changes in the dynamics of neural activity, in the artificial networks. Specifically, dynamic attractors became deeper and more robust to perturbations. We have also examined similar dynamics in task related EEG data, collected at multiple time points across adolescence, and found that similar changes can be found in the neurophysiology data. This supports the hypothesis that adolescent synaptic pruning leads to increasingly robust recurrent computations, which supports improvements in goal-directed behaviors.

Josh Brown Indiana University

fMRI studies of non-invasive deep brain temporal-interference neurostimulation in humans

There are several existing methods of non-invasive neurostimulation in humans, including transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), transcranial magnetic stimulation (TMS) and transcranial focused ultrasound (tFUS). Whey they have their advantages, they are limited in the ability to stimulate deep brain regions without also stimulating the overlying cortex. A number of neural targets for both scientific and therapeutic purposes are thus outside the range of what can be studied non-invasively. A new neurostimulation method (temporal interference electrical neurostimulation, TI) may resolve this problem by triangulating interference patterns generated by multiple alternating current sources. This has been shown to cause changes in neural activity in rodents (Grossman et al., 2017). We have further investigated whether and how accurately we can stimulate deeper brain regions with combined TI and fMRI. In a series of human subjects, we computed optimal electrode locations to target the nucleus accumbens (NAcc) and tested for BOLD effects with fMRI. The results show strong BOLD effects near the targeted region, but with some variability, and that these effects are specific to the electrical interference pattern rather than to the individual alternating currents separately. The results suggest a promising new method for studying the causal role of deeper brain regions in cognitive processes.

Johannes Burge University of Pennsylvania

Temporal processing and 3D vision

I will discuss recent results demonstrating striking perceptual consequences when different visual features and different visual locations are processed with millisecond-scale differences in timing. Certain image differences between the eyes cause dramatic misperceptions of where in 3D space a target is and in what 3D direction it is moving; and these effects are modulated by where in the visual field a target is located. I will explain the temporal processing and stereo-geometry underlying these misperceptions. The fact that substantial perceptual errors are caused by millisecond differences in processing speed highlights the exquisite temporal calibration required for accurate perceptual estimation. The fact that these misperceptions are rare in natural viewing indicates how well the visual system is calibrated in normal circumstances. Ongoing and future work on a range of related topics with clinical and scientific import will be discussed.

Matthew Chafee University of Minnesota

Spike timing and prefrontal circuit disconnection in schizophrenia models

Abstract: Current theories of schizophrenia suggest that over-pruning of synapses during late adolescence disconnects prefrontal local circuits, disrupting the computations they perform and producing cognitive deficits in the disease. In this talk, I will describe evidence from our lab in animal and computational models that a disruption of neural synchrony, specifically synchronous spiking between neurons, may drive circuit disconnection in an activity-dependent manner in the human disease. We show that blocking NMDAR in monkeys (a synaptic deficit implicated in schizophrenia) and deleting a schizophrenia risk gene in mice (Dgcr8) produce convergent disruptions in synchronous spiking in prefrontal local circuits, coupled with functional disconnection of these circuits. We further present results from a spiking neural network model that provides a mechanistic explanation for these results, linking reduced synchronous spiking at the neural level to reduced oscillatory activity at the population level following NMDAR blockade. Together, these results combine to provide a view of pathogenesis of schizophrenia in which disruptions in activity timing drive disconnection and malfunction of prefrontal local circuits.

Daniel Wonjae Chung University of Pittsburgh

Combining postmortem studies and computational modeling to decipher cortical circuit abnormalities in schizophrenia

Background: Cognitive symptoms in schizophrenia (SZ) are associated with deficits in synchronous neural activity at gamma frequency in the prefrontal cortex (PFC). Lower PFC gamma power in SZ is proposed to arise due, in part, to altered excitatory drive to parvalbumin-containing interneurons (PVIs), but the nature of alterations underlying this process is unknown. Here, I will discuss findings from our postmortem and computational modeling studies that demonstrate the pathological basis of altered excitatory drive to PVIs and their impact on PFC gamma power in SZ. Then, I will discuss applying the new high-resolution technique of expansion microcopy to postmortem studies to uncover novel alterations in excitatory drive to PVIs in SZ.

Methods: The density of VGlut1+/PSD95+ puncta on PVIs and the puncta levels of VGlut1 and PSD95 were quantified to assess the number and the strength, respectively, of excitatory inputs to PVIs in PFC of 20 matched pairs of SZ and comparison subjects. The impact of synaptic alterations on gamma power was first assessed in a small-scale model network and then validated in a large-scale model network. Finally, 10X expansion microscopy was performed to assess the assembly of synaptic proteins (e.g., RIM, PSD95, GluA) within excitatory synapses in human PFC.

Results: The mean number of excitatory inputs to PVIs was lower in PFC of SZ relative to comparison subjects. The mean strength of remaining inputs did not differ, but the variability of excitatory synaptic strength across PVIs was greater in PFC of SZ. Simulating these alterations in both small- and large-scale model networks showed that each alteration mildly reduces gamma power, but synergistically interacts with other synaptic alterations to substantially reduce gamma power. Finally, 10X expansion microscopy showed that pre- and postsynaptic proteins organize into clusters and align trans-synaptically, revealing the molecular architecture of excitatory synapses in human PFC.

Conclusions: Here, we combined postmortem studies and computational modeling to demonstrate altered mean and variability of excitatory synaptic strength across PVIs in SZ and predict their impact on gamma power in model networks. Developing new tools to unmask synaptic architecture of human PFC circuitry may provide further insights into the nature of alterations in excitatory drive to PVIs in SZ.

Anne Churchland UCLA

What determines decision accuracy in rats, mice and humans?

Traditional studies of perceptual decision-making typically assume that choices as based mainly on sensory evidence and priors. We uncovered two new features that contribute to decision accuracy in multiple species. First, we find that when stimuli are uncertain, subjects have a tendency to explore stimulus-choice contingencies, leading to non-zero lapse rates. We found that the magnitude of lapse rates was smaller for multisensory choices, leading us to consider whether action value modulated the rate of subjects' exploration. We tested this explicitly by increasing the action value on one side, and observed a decrease in lapse rate only on that side. Second, we observe that subjects' decision accuracy is non-stationary over an experimental session. Hidden markov models were better able to account for choice accuracy when they assumed that decision-making performance was governed by 2-4 "states", including a highperformance "engaged" state and several disengaged or biased states. To better understand what drives disengaged states, we studied how spontaneous, uninstructed movements fluctuate over the course of a session. We found that although task irrelevant movements are generally more plentiful during disengaged states, a small subset of movements restricted to the delay period were frequent when the animal was highly engaged. Taken together, these observations point to a new framework for understanding decision-making that includes nonstationary engagedment levels, uncertainty guided exploration and a careful consideration of diverse movements.

Mark Churchland Columbia University

From spikes to factors: understanding large-scale neural computations

It is widely accepted that human cognition is the product of spiking neurons. Yet even for basic cognitive functions, such as the ability to make decisions or prepare and execute a voluntary movement, the gap between spikes and computation is vast. Only for very simple circuits and reflexes can one explain computations neuron-by-neuron and spike-by-spike. This approach becomes infeasible when neurons are numerous the flow of information is recurrent. To understand computation, one thus requires appropriate abstractions. An increasingly common abstraction is the neural 'factor'. Factors are central to many explanations in systems neuroscience. Factors provide a framework for describing computational mechanism, and offer a bridge between data and concrete models. Yet there remains some discomfort with this abstraction, and with any attempt to provide mechanistic explanations above that of spikes, neurons, cell-types, and other comfortingly concrete entities. I will explain why, for many networks of spiking neurons, factors are not only a well-defined abstraction, but are critical to understanding computation mechanistically. Indeed, factors are as real as other abstractions we now accept: pressure, temperature, conductance, and even the action potential itself. I use recent empirical results to illustrate how factor-based hypotheses have become essential to the forming and testing of scientific hypotheses. I will also show how embracing factor-level descriptions affords remarkable power when decoding neural activity for neural engineering purposes.

-----Patricia Churchland UCSD

The Neurobiological Platform for Moral Behavior

Social neuroscience, especially in the last decade, has made impressive progress in exploring the neural mechanisms regulating social behavior, including consolation behavior, attachment and bonding, aggression, willingness to punish, and the effects of nurturing and social stress on the developing brain. In parallel, behavioral research on nonhuman mammals and birds has revealed the existence of prosocial choice, consolation behavior as well as altruistic behavior. In combination, the research raises the wider question of what these various results signify for our understanding of human social motivation in general and moral motivation in particular. Although moral philosophers have discussed norms and values since Socrates and Confucius, the scientific approach has provided new insights and provoked a reconsideration of common assumptions about the nature and origin of moral values. This talk has five parts: (1) the evolutionary origin of sociality in mammals and birds, (2) a brief geography of moral philosophy (3) presentation of selected highlights from social neuroscience, (4) discussion of the links between the reward system and reinforcement learning of social norm and (5) what this all means for understanding moral values.

Alberto Cruz-Martin Boston University

Cell Type Specific Contributions to Anxiety Deficits in a Mouse Model of Complement 4 Overexpression

Schizophrenia (SCZ) is a devastating mental illness without satisfactory treatment options. Among the clinical traits of SCZ are cognitive impairments such as deficits in attention and working memory, traits which suggest medial prefrontal cortex (mPFC) dysfunction. Lower levels for markers of inhibitory neurons and decreased density of excitatory synapses on GABAergic parvalbumin-positive interneurons (PV-INs) in postmortem mPFC tissue suggest that alterations in specific inhibitory mPFC microcircuits could underlie SCZ pathophysiology. PV-INs play a unique function in regulating pyramidal neuron (PN) spiking patterns and orchestrating brain oscillations, suggesting that they are critical for proper cognitive function. PV-INs are especially susceptible to developmental stressors, and transient developmental perturbations in their activity lead to long-lasting deficits in the function of the mPFC, including abnormalities in connectivity and gamma oscillations. Although it is not completely understood, developmental alterations in PV-IN function could result in perturbations in cortical maturation or activation of compensatory mechanisms that ultimately lead to long-lasting circuit changes. However, SCZ is a highly heritable disease, and there are very few studies linking specific manipulations of SCZ-associated genes to PV-IN dysfunction.

In humans, specific structural variants of immune gene, C4A, increase C4A expression and confer greater risk for developing SCZ. Our group demonstrated that overexpression of C4A (C4-OE) in mPFC pyramidal neurons led to alterations in synaptic developmental wiring and induced social behavioral deficits in mice. However, our preliminary data using M-FISH in the mPFC suggest that PV-INs are a cellular source of C4. We hypothesize that specific C4-OE in PV-INs reduces the excitatory drive on this developmentally-vulnerable interneuron type, and this is sufficient to cause long-term deficits of mPFC-associated behavior. To test this hypothesis, we have developed a novel, conditional C4-OE mouse line and have crossed this to PV-Cre driver mice. Our preliminary data suggest that C4-OE exclusively in PV-INs is sufficient to cause a sexually dimorphic anxiety-like behavioral deficit. Our goal is to determine the mechanistic role of C4-OE in PV-INs in driving the pathology that underlies the observed anxiety-like deficits, at the synaptic level.

Fulvio Domini Brown University

A "novel" non-probabilistic model of 3D cue integration explains both perception and action

The pentagonal faces of a soccer ball or the smooth surface of an egg reflect light patterns that are readily perceived as three-dimensional shapes. Yet, each object projects different 3D signals. The regular pattern of projected pentagons from the ball form on the retina a compelling texture gradient. The unmarked surface of the egg, however, only a shading gradient. Traditionally, the presence or absence of image signals reflected by various objects in a scene has been modelled in terms of signal reliability. According to this view, each signal is used to compute a probability distribution of possible depth interpretations, which is on average peaked at the veridical value. If signals are reliable, like the texture gradient projected by the ball, then this distribution is narrow. The Maximum Likelihood approach of cue integration combines the depth estimates from all the signals by factoring in their reliabilities, guarantying a final estimate that is maximally reliable. Although the MLE approach is a rational choice, it is still not clear how signal reliabilities are estimated and how the visual system can learn a veridical mapping between image and 3D properties. In this talk, I will present a model that does not depend on these assumptions. Instead, I postulate that the visual system learns a fixed mapping between image signals and depth through a deterministic function that maximizes the sensitivity to depth while minimizing its response to random fluctuations of image signals. I will illustrate how this model can account for previous results, but also predict novel findings that are incompatible with the MLE account of 3D cue integration.

James Elder York University

Single-view 3D perception in humans and machines

While multi-view cues such as stereo and motion parallax are important to 3D perception, humans still perceive objects and scenes in 3D when viewed in a single image or at distances where stereopsis and motion cues are weak. How do our brains do this? While deep networks can be trained to recover 3D range from a single image, these systems struggle to capture the crisp structures that humans perceive, and with millions of free parameters provide little insight into the geometry and computational principles that underpin monocular 3D perception.

For a deeper insight into these principles, recall the revolution in picture creation that emerged in the early Renaissance with the discovery of the geometric rules of perspective projection. These rules connect simple 2D cues in the picture plane (e.g., vanishing points), to 3D properties of surfaces (e.g., 3D orientation) based on relatively general regularities in the 3D scene (e.g., parallelism, rectilinearity).

In this talk I will explore the use of these perspective projection cues by both humans and machines for single-view 3D perception. In lieu of high-dimensional black-box deep networks, I will focus on more explainable low-dimensional models that can be explicitly related to the underlying geometry and statistics of our visual world and can be applied to a range of problems in 3D urban scene understanding.

Roland Fleming University of Gissen

Learning to see stuff

Humans are very good at visually recognizing materials and inferring their properties. Without touching surfaces, we can usually tell what they would feel like, and we enjoy vivid visual intuitions about how they typically behave. This is impressive because the retinal image that the visual system receives as input is the result of complex interactions between many physical processes. Somehow the brain has to disentangle these different factors. I will present some recent work in which we show that an unsupervised neural network trained on images of surfaces spontaneously learns to disentangle reflectance, lighting and shape. We find that the network not only predicts the broad successes of human gloss perception, but also the specific pattern of errors that humans exhibit on an image-by-image basis. We argue this has important implications for thinking about vision more broadly.

Michael Frank Brown University

Beyond drift diffusion: fitting a broad class of neurally informed decision making models with likelihood approximation networks

Computational modeling can formally adjudicate between theories and affords quantitative fits to behavioral/brain data. This talk has two parts: in the first I describe an example of how simplified models of brain function can be useful for linking neural circuits to decision making functions. The models provide a mechanistic interpretation of changes in decision making in patient populations. However, for quantitative fitting purposes, the space of plausible generative models considered is dramatically limited by the set of models with known likelihood functions. For many models, the lack of a closed-form likelihood typically impedes Bayesian inference methods. As a result, standard models like the drift diffusion model are often fit to data for convenience even when other models might be superior. In the second part of the talk I will present a new method using artificial neural networks that learn approximate likelihoods for arbitrary generative models, allowing fast posterior sampling with only a one-off cost for model simulations that is amortized for future inference. We show that these methods can accurately recover posterior parameter distributions for a variety of neurocognitive process models. We provide code allowing users to deploy these methods for arbitrary hierarchical model instantiations linking brain mechanisms to behavior and for interrogating alterations in patient populations.

Brian Garibaldi Johns Hopkins

Applying Precision Medicine to COVID-19

The Johns Hopkins Biocontainment Unit (BCU) is a federally funded Regional Emerging Special Pathogens Treatment Centers (RESPTCs), designed to care for patients infected with high consequence pathogens. The BCU was one of the first teams to care for COVID-19 patients in Maryland and played an important role in both clinical care and research on COVID-19. The BCU team established the JH-CROWN data registry which includes more than 15,000 COVID-19 inpatients and 150,000 COVID-19 outpatients. This effort led to the establishment of the Johns Hopkins Precision Medicine Center of Excellence (PMCOE) for COVID-19. The COVID-19 PMCOE has conducted comparative effectiveness analyses demonstrating the real-world benefits of therapeutics such as remdesivir, tocilizumab, and high-flow nasal cannula and developed real-time prediction models for COVID-19 clinical trajectories used by frontline clinicians around the world. The COVID-19 Inpatient Risk Predictor (CIRC) is featured on MDCalc, one of the most widely used medical resource sites. The Severe COVID-19 Adaptive Risk Predictor (SCARP) is currently live in the Epic electronic health record where it gives Hopkins frontline providers real-time predictions about the likelihood of a patient developing severe disease or death from COVID-19. The PMCOE has also examined racial disparities in COVID-19. The PMCOE team demonstrated that pulse oximetry systematically overestimates oxygenation in African American patients, which in turn leads to a delay in recognizing individuals who are eligible for COVID therapies. The fact that the COVID-19 PMCOE was able to develop a new registry during a pandemic and then translate key clinical findings into tangible point-of-care tools is a wonderful realization of the promise of precision medicine.

Jovan Kemp Brown University

Evidence that Just-Noticeable Differences do not reflect perceptual uncertainty in depth discrimination

The Just-Noticeable Difference (JND) measures the minimum difference in an experimentally varied comparison stimulus that can be reliably discriminated from a fixed standard stimulus. However, whether the JND emerges solely from noise in perceptual encoding, as is conventionally assumed, or reflects something else entirely remains an important empirical question. For 3D shape perception, the JND is used as a proxy measure of uncertainty emerging from depth cue encoding. This interpretation is based on two assumptions: (1) the slope of the perceptual function relating physical to perceived depth is unitary and (2) perceptual uncertainty yields noisy depth estimates. Here we provide evidence against these two assumptions and propose an alternative model which both accounts for previous JND findings and makes new predictions. We hypothesize that (1) the slope of the perceptual function is not unitary but depends on the strength of the depth cue, (2) depth perception is deterministic and does not yield noisy depth estimates, and (3) the noise affecting discrimination is task related and independent of depth processing. We posit that the slope of the perceptual function determines the JND: if the slope is small, a large change of physical depth is necessary to bring about a discriminable change in perceived depth. The JND is therefore entirely dependent on the experimentally varied comparison stimulus since the standard stimulus is fixed and yields a noiseless depth estimate. To test the JND's dependence on the comparison, we designed a novel method where we independently vary the strength of the standard stimulus and the comparison stimulus. The strength of the stimuli was weakened through one of two means: by manipulating the gradients within a cue or by removing a cue from a multi-cue display. Remarkably, we find that the JND only depends on the comparison stimulus: stronger comparison stimuli cause smaller JNDs. Conversely, the JND was independent from the nature of the standard stimulus. Altogether, the findings provide evidence that the JND does not reflect depth cue uncertainty and instead reflects deterministic perceptual functions.

Yevgenia Kozorovitskiy Northwestern University

Dopamine dynamics and neuroplasticity across behavioral states

Neuromodulatory signaling complements fast neurotransmission in the mammalian brain, and it is broadly critical for neurodevelopment and in mental health. With a focus on basal ganglia and dopamine during learning, we examine our laboratory's recent data revealing tunable changes in dopaminergic signaling after aversive learning. These changes in the ventral tegmental area dopamine neurons can predict the behavioral effects of future experience and responses to rapidly acting anti-depressant medications, such as ketamine. Ketamine, by recovering appropriate dopamine signatures, appears to facilitate dendritic spine and synapse plasticity in the medial prefrontal cortex to recover behavioral flexibility. We also review recent advances in miniaturized wireless applications, developed through large-scale collaborative work to advance ethologically grounded behavioral neuroscience studies in groups of animals or in complex physical spaces. Until recently, limited programmable control and narrow options in illumination profiles constrained the use of such existing devices. Here, real-time independent control of optogenetic stimulation through near-field communication dramatically expands the realm of applications of these devices in neuroscience, building the framework for integration of additional sensing modalities and powerful options for closed-loop control of neuromodulation.

Mike Landy NYU

Sensory-motor confidence

We constantly evaluate our actions for success, both as a form of internal reward and to guide motor learning. We ask, what sensory and motor-execution cues are used in making these judgements and when are they available? There are two temporally distinct sources of information to guide a confidence judgment: prospective cues, which are available prior to the action (e.g., knowledge of motor noise and past performance), and retrospective cues specific to the action itself (e.g., proprioceptive measurements of limb position and visual feedback, when available). We investigated which of these two cues were used in two tasks, a motor-awareness task and a confidence-judgment task. In both tasks, participants reached toward a visual target with an unseen hand. In the motor-awareness task, they indicated with a visible cursor where they thought they landed. In the confidence-judgment task, they made a continuous judgment of confidence about the success of the reach. The confidence judgment was incentivized so as to motivate accurate reaches and attentive reporting to maximize their score. We compared three Bayesian-inference models of sensorimotor confidence based on either prospective cues, retrospective cues, or both sources of information. Each model chose the confidence response that maximized expected gain given the available information. Our findings showed two distinct strategies: participants either performed as ideal observers, using both prospective and retrospective cues to make the confidence judgment, or relied solely on prospective information, ignoring retrospective cues. Participants made use of retrospective cues in the motor-awareness task, but these cues were not always included in the computation of sensorimotor confidence.

This work was carried out with Marissa Fassold and Shannon Locke. Support: NIH EY08266

Tim McNamara Vanderbilt University

Bayesian priors in spatial memory and spatial causal inference

Spatial navigation is a complex cognitive activity that depends on perception, action, memory, reasoning, and decision making. Effective navigation depends on the ability to use information from multiple spatial cues to estimate one's position and the locations of goals. Spatial cues include landmarks, and other visible features of the environment, and body-based cues generated by self-motion (vestibular, proprioceptive, & efferent information). Navigators need to decide how to use the information provided by multiple spatial cues, and when the cues conflict, they must determine whether the disparities are caused by error in sensory-perceptual systems or by different sources in the world. Preliminary findings from our lab indicate that navigators' memories of the locations of objects in a large arena are not biased by prior experience and that their causal inferences in a homing task are not influenced by objective causal probabilities in the manner predicted by Bayesian decision models.

David Melcher NYU

The role of prediction in naturalistic visual perception

Hypotheses concerning the neurological basis of dyslexia include dysfunction of the magnocellular system in the brain, abnormal temporal processing, and/or deficient phonological skills. Each of these theories has merit, but the link among them has not been identified. Here we show that people with dyslexia have a selective impairment in the magnocellular portion of the medial geniculate nucleus, the auditory relay in the thalamus. We used functional magnetic resonance imaging to measure highly consistent and profoundly attenuated responses to non-linguistic transient but not sustained sounds compared to normal readers. This measurement is a 95% accurate diagnostic for dyslexia in individual subjects. Our finding identifies a core deficit causing dyslexia that can unify the three hypotheses.

Cory Miller UCSD

Cross-Modal Representation of Identity in Primate Hippocampus

Faces and voices are the dominant social signals used to recognize individuals amongst human and nonhuman primates. Yet, how little remains known about how these critical signals are integrated into a modality-independent representation of individual identity in the primate brain. Here we show that, like humans, single neurons in the marmoset monkey hippocampus exhibit invariant neural responses when presented with the faces or voices of conspecifics. However, we also discovered a robust parallel mechanism for representing cross-modal identities in which single neurons and a population code in hippocampus were responsive to the faces and voices of multiple conspecifics. Manifold projections likewise showed separability of individuals, as well as clustering for family members, suggesting that multiple learned social categories are encoded as related dimensions of identity in hippocampus. The findings reveal that neural representations of identity in hippocampus are not only cross-modal but organized based on respective social relationships.

Jeff Mulligan Freelance

Internet-based methods for assessing data literacy

Many day-to-day decisions can profitably be informed by data. Sometimes the necessary data may be obtained by direct observation, such as deciding whether or not to carry an umbrella by looking out of the window at the sky. But often the data informing important decisions have been collected by others. In such cases, optimal decision making depends upon effective communication to enable accurate interpretation of the data. But how can we assess whether or not these data communications have succeeded? In this talk we present a novel technique for assessing comprehension of a summary graph by asking participants to report their internal model of the underlying raw data. Initial results and possible generalizations of the technique will be discussed.

Katherine M. Nautiyal Dartmouth College

It's not just dopamine - Serotonin also modulates brain reward systems

Although dopamine is best known for its role in regulating reward signaling in the brain, the neurotransmitter serotonin also influences reward processing and goal-directed behavior, though the mechanisms are much less understood. A recently developed biosensor allows us to measure serotonin levels in the brain on a timescale consistent with understanding how serotonin encodes single rewards. We focused on striatal brain regions given their known roles in processing reward and regulating goal-directed behavior. We see a robust increase in serotonin release that precedes the consumption of reward and is graded by reward value. Although it seems to be an anticipatory reward signal, the serotonin release does not encode a cue that predicts a reward. Further, we used miniature microendoscopes for calcium imaging of dorsal striatal medium spiny neurons (MSNs) in adult mice during goal directed behavior to determine the role of serotonin release in modulating the neural activity in the striatum. We analyzed changes in calcium event rates in D1- and D2-expressing MSNs during the different phases of reward seeking behavior and in response to an increased palatable reward. We find that the majority of cells decrease their calcium activity to reward-predicting cues and reward delivery, and that this inhibition is abolished in the absence of the serotonin 1B receptor, suggesting that serotonin is being released in anticipation of reward and inhibiting striatal neural activity through the 1B receptor. Our results are important for understanding the neural encoding of rewards and action and how it may be modulated by the serotonin system.

Cris Niell University of Oregon

Neural circuits for natural behavior and active vision in the mouse

In the natural world, animals use vision to analyze complex scenes and enable a wide range of visually-driven behaviors, many of which require movement through the environment. However, in practice most studies of vision are performed in stationary subjects performing artificial tasks in response to simple stimuli. In order to bridge this disconnect between how vision is actually used and how it is studied in the lab, we are investigating the neural circuits mediating ethological behaviors that mice perform. We have developed two behavioral paradigms, prey capture and gap crossing, that have provided insight into behavioral strategies and neural circuits for detection of relevant stimulus features within a complex and dynamic sensory environment. We have also implemented novel experimental approaches to measure neural coding of the visual scene as animals freely move through their environment, which has revealed the impact of movement-related signals and active sampling on visual processing.

Zyg Pizlo & Mark Beers UC Irvine

Recovering shapes of 3D real objects from a single image.

The problem of mapping from a 2D image to a 3D perceptual interpretation is severely underconstrained (for a long time considered unsolvable). The visual system must infer the lost depth dimension. A priori constraints (aka priors) for the missing depth dimension seem to be required, but effective depth constraints don't exist. Assigning a prior to depths of points, edges and surfaces of a 3D object is unrealistic because these depths change when the object's 3D position and orientation change. So, depth constraints are not likely to be helpful in 3D shape perception. Binocular vision could remedy this problem, but we will show that monocular 3D shape perception is as good as binocular shape perception.



We used models of 3D natural shapes from <u>https://modelnet.cs.princeton.edu/</u>. The graph above shows performance of a subject in a 3D shape recovery task when presented either orthographic or perspective images of natural shapes. The x-axis is a binary logarithm of the ratio of aspect ratios of the recovered 3D shape and the reference (veridical) shape. The vertical axis is the cumulative distribution of the shape difference. The median error (50th percentile) for this subject when viewing perspective images was 12%. These results show that human observers see 3D natural shapes veridically, or nearly so. Our computational model that emulates human performance uses three a priori constraints: mirror symmetry, compactness and rectangularity.

Meri Rosen NE Ohio Medical University

Prolonged development of duration discrimination: Human perception and neural correlates

The perception of temporally-varying sounds, which is important for comprehending speech, matures over an extended developmental period. Elucidating the normal maturational trajectory of such perception and its neural substrates provides a basis for understanding perceptual difficulties that arise from auditory processing issues. One element of temporal processing is duration discrimination, which enables the accurate identification of consonants and vowels. For example, distinguishing 'buck' vs 'bug' (voiced vs non-voiced offsets) relies on accurately perceiving the vowel duration. Auditory cortical (ACx) responses mature well into adolescence, and the ACx is necessary for the perception of temporally-varying sounds. Thus across development, we separately examined and compared perceptual duration discrimination in humans, with ACx duration discrimination in an established animal model for auditory processing, the Mongolian gerbil. This allowed us to determine which elements of ACx firing patterns matured in conjunction with perceptual maturation. We recorded responses to varying duration sound bursts (10, 30, 50, 100, or 200 ms) from primary ACx of juvenile (postnatal day (P) 25-30) and adult (P90-P130) awake, head-fixed gerbils. Neurons responded with either onset or sustained firing patterns to these sounds, and sustained response types were more common in juveniles compared with adults (62% vs 47%). Only the sustained cells discriminated amongst sound durations. Yet in juveniles, these duration-sensitive sustained cells did not distinguish durations as well as adult cells. From these neurons, we created neurometrics mimicking decoding from a downstream recipient neuron. Neurometrics revealed an age-based improvement in duration discrimination based on the response duration (RD) but not the firing rate (FR) of sustained neurons.

To compare these neurometrics with perception across development in humans, listeners aged 8-19 years discriminated between varying duration sound bursts (using a 3-alternative forced choice procedure). Duration discrimination performance continued to develop well into adolescence, up to age \sim 14 years. Across development, psychometric functions were best matched with neurometrics from sustained rather than onset cells, and in particular with RDs rather than FRs of these sustained cells. Thus, extended firing patterns from a subset of ACx neurons likelly contribute to the extended developmental trajectory of duration discrimination.

Measuring agency

The development of new therapeutic methods for intervening in brain function have the potential to influence a person's autonomy and authenticity. In order to determine whether or not this is the case, we need an assay that can measure aspects of agency before and after neurointervention. Here I introduce a framework for thinking about agency as a multidimensional construct, and describe a research project aimed at measuring agency. We develop an Agency Assessment Tool (AAT) using survey and behavioral methods. I present preliminary results from the project that show that the AAT is able to discern control and patient groups, and discuss the prospects for using data-driven tools to come up with ontologies of agency.

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Influences of eye movements on stereopsis

Humans use differences in the visual input to the two eyes to extract depth information, a process known as stereopsis. The visual system is exquisitely sensitive to these differences and able to detect disparities smaller than the photoreceptor spacing. This accomplishment is even more remarkable considering that the eyes drift incessantly during fixation, resulting in retinal image motions that are largely uncorrelated in the two eyes. Since these drifts cover tens of photoreceptors and continually change the correspondence between retinal points, one might expect they would hinder stereopsis. Here we present recent evidence supporting the opposite hypothesis: disparity modulations resulting from ocular drifts are, in fact, beneficial. We show that stereoscopic judgments are greatly impaired when the images in both eyes are continually adjusted to counteract the visual consequences of eye drifts so to eliminate disparity modulations. Our results extend dynamic theories of vision to depth perception. They suggest that stereoscopic perception relies on transient disparity signals produced by fixational eye movements.

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Keith Schneider

A profound attenuation of auditory transients in the magnocellular medial geniculate nucleus in dyslexia is a potential neuroimaging diagnostic in individual subjects

Hypotheses concerning the neurological basis of dyslexia include dysfunction of the magnocellular system in the brain, abnormal temporal processing, and/or deficient phonological skills. Each of these theories has merit, but the link among them has not been identified. Here we show that people with dyslexia have a selective impairment in the magnocellular portion of the medial geniculate nucleus, the auditory relay in the thalamus. We used functional magnetic resonance imaging to measure highly consistent and profoundly attenuated responses to non-linguistic transient but not sustained sounds compared to normal readers. This measurement is a 95% accurate diagnostic for dyslexia in individual subjects. Our finding identifies a core deficit causing dyslexia that can unify the three hypotheses.

Thomas Serre Brown University

Recurrent neural circuits for perceptual grouping

Neurons in the visual cortex are sensitive to context: Responses to stimuli presented within their classical receptive fields (CRFs) are modulated by stimuli in their surrounding extra-classical receptive fields (eCRFs). However, the circuits underlying these contextual effects are not well understood, and little is known about how these circuits drive perception during everyday vision. We tackle these questions by approximating circuit-level eCRF models with a differentiable discrete-time recurrent neural network that is trainable with gradient-descent. After optimizing model synaptic connectivity and dynamics for object contour detection in natural images, the neural-circuit model rivals human observers on the task with far better sample efficiency than state-of-the-art computer vision approaches. Notably, the model also exhibits CRF and eCRF phenomena typically associated with primate vision. The model's ability to accurately detect object contours also critically depends on these effects, and these contextual effects are not found in ablated versions of the model. Finally, we derive testable predictions about the neural mechanisms responsible for contextual integration and illustrates their importance for accurate and efficient perceptual grouping.

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Predictive decoding of the auditory mind

Perception and Action engage extensive sensory and motor interactions with predictive signals playing the major role in skill learning and cognition. I shall briefly describe ECoG recordings of such responses during speech vocalizations and discuss the role of the auditory-motor mappings in learning how to speak. These results are then generalized to sensory perception and imagination of music and speech with EEG and MEG recordings, leading to a brief account of how to decode imagined music and speech from these non-invasive signals.

Sharad Shanbhag NE Ohio Medical University

Representations of Social Vocalizations in the Basolateral Amygdala of Big Brown Bats

In vertebrate acoustic communication, the sequencing and temporal emission pattern of vocalizations convey information about the animal's state and affects the state of a listening animal. Our work describes responses to natural vocal stimuli in adult big brown bats (Eptesicus *fuscus*). We first assessed how vocal sequences correlate with the internal state (heart rate, HR) and behavior of the sender and modify the internal affective state of a listener (via heart rate). We then characterized neuronal responses in the basolateral amygdala (BLA) of awake, restrained bats to vocal sequences and isolated syllables. On the basis of background firing rates, we distinguished two populations of BLA neurons that also differed in selectivity for vocal stimuli. Low background neurons (<1 spike/s) displayed high selectivity, responding on average to one tested stimulus. These may participate in a sparse code of vocal stimuli, in which each neuron responds to one or a few stimuli, and the population responds to the range of vocalizations across behavioral contexts. In contrast, neurons with higher background rates (>1 spike/s) responded broadly to tested stimuli. Such neurons better represented the timing of syllables within sequences, and spike timing information improved the ability of these neurons to discriminate among vocal sequences, and among the behavioral contexts associated with sequences, compared to a rate code alone. Intracellular recordings revealed that most BLA neurons show postsynaptic responses to multiple vocalizations but that many fewer neurons show spiking responses, and these are more selective. Further, vocal stimuli associated with either positive or negative valence are similarly effective in eliciting EPSPs, IPSPs, and spiking responses. These findings demonstrate that the BLA contains distinct representations of vocal stimuli and that BLA neurons can provide a basis for emotional/physiological responses to these stimuli. Further, the greater selectivity of spiking responses than PSP responses suggests an integrative process within the BLA to enhance response specificity.

George Sperling UC Irvine

Discovering how many salience maps we have

Koch and Ullman (Human Neurobiology, 1985) proposed a 2D topographical salience map that took feature-map outputs as its input and represented the importance "saliency" of the feature inputs at each location as a real number. The computation on the map, "Winner-Take-All," was used to predict action priority. We propose that the same or a similar map is used to compute centroid judgments, the center of a cloud of diverse items. Sun, Chu, and Sperling (Attn, Perc, & Psychophys., 2021) demonstrated that following a 250 msec exposure of a 24-dot array of 3 intermixed colors, subjects could accurately report the centroid of each dot color, thereby indicating that these subjects had at least three salience maps. Here, we use a post-cue, partialreport paradigm to determine how many more salience maps subjects might have. In 11 experiments, subjects viewed 0.3 sec flashes of 28 to 32 item arrays composed of M, M=3,...,8, different features followed by a cue to mouse-click the centroid of items of just the post-cued feature. Ideal detector response analyses show that subjects utilized at least 12-17 stimulus items. By determining whether a subject's performance in (M-1)-feature experiments could/could-not predict performance in M-feature experiments, we conclude that one subject has at least 7 and the other two have at least 5 salience maps. A computational model shows that the primary performance-limiting factors are channel capacity for representing so many concurrently presented groups of items and working-memory capacity for so many computed centroids.

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Ensemble Perception: perception of Mean and Variability

Ensemble perception provides a visual summary of a scene, such as the mean size of a group of objects. The precise mechanisms underlying ensemble perception are still unknown. We tested whether different types of ensemble tasks rely on or compete for shared processes. Perception of the mean requires extracting the similarities across the display, whereas perception of variability requires extracting the differences. We tested whether judging both mean and variability would exert a cost on perceptual sensitivity. An array of circles of different sizes briefly flashed on the screen, and participants (N = 315) judged the mean, variability, and/or numerosity of the display. Participants were less sensitive to mean judgments when also judging the variability. Sensitivity to variability was similar regardless of whether participants also judged the mean. These asymmetrical results suggest that the mean is automatically perceived when judging variability, and thus there is no additional cost to also reporting the mean. However, variability is not automatically perceived when judging the mean, suggesting a cost to also reporting variability. In statistics, calculations of both the mean and the variability require a measure of the number of samples. We explored whether the perception of variability also required perception of the number of samples, in which case, there should be no cost to also judging the number of items. Sensitivity to variability was unaffected when also making a judgment of the number of items. When perceiving variability, judgments of other ensemble properties such as mean and numerosity do not impair variability judgments. In contrast, sensitivity to the mean circle size and numerosity were both impaired when also having to judge variability. Overall, these results show an asymmetrical process underlying ensemble perception, suggesting that ensemble perception could be driven by domain-specific mechanisms dependent on the type of summary statistic computed.