Columbia Workshop on Brain Circuits, Memory and Computation

Monday and Tuesday, March 13-14, 2017 | Davis Auditorium, CEPSR

Organizer and Program Chair: Aurel A. Lazar (Columbia University)

The goal of the workshop is to bring together researchers interested in developing executable models of neural computation/processing of the brain of model organisms. Of interest are models of computation that consist of elementary units of processing using brain circuits and memory elements. Elementary units of computation/processing include population encoding/decoding circuits with biophysically-grounded neuron models, non-linear dendritic processors for motion detection/direction selectivity, spike processing and pattern recognition neural circuits, movement control and decision-making circuits, etc. Memory units include models of spatio-temporal memory circuits, circuit models for memory access and storage, etc. A major aim of the workshop is to explore the integration of various sensory and control circuits in higher brain centers.

Program Overview

Monday 09:00 AM - 05:30 PM

09:00 AM - 09:45 AM **Gerald M. Rubin** (HHMI Janelia), Circuits for Learning and Memory in the Adult *Drosophila* Mushroom Body

09:45 AM - 10:30 AM **Ann-Shyn Chiang** (National Tsing Hua U.), Long-Term Memory Requires Sequential Protein Synthesis in Discrete Mushroom Body Output Neurons in *Drosophila*

10:30 AM - 11:00 AM Coffee Break

11:00 AM - 11:45 AM **Albert Cardona** (HHMI Janelia), Brain Circuit Maps of Larval *Drosophila*

11:45 AM - 12:30 PM **Andreas S. Thum** (University of Konstanz), The Larval Standard Brain of *Drosophila*: The Mushroom Body Learning and Memory Network

12:30 PM - 02:00 PM Lunch Break

02:00 PM - 02:45 PM **Silke Sachse** (Max Planck Institute for Chemical Ecology), Parallel Olfactory Coding Mechanisms in the *Drosophila* Brain

02:45 PM - 03:30 PM **Dinu Florin Albeanu** (Cold Spring Harbor Laboratory), Understanding the Function and Specificity of Feedforward and Feedback Signals in Olfaction

03:30 PM - 04:00 PM Afternoon Break

04:00 PM - 04:45 PM **Vijay Balasubramanian** (University of Pennsylvania), Cracking the Olfactory Code

04:45 PM - 05:30 PM **Konrad P. Kording** (Northwestern University), Deep Learning and the Unknown Unknowns of Neuroscience

Tuesday 09:00 AM - 05:30 PM

09:00 AM - 09:45 AM **Barry J. Dickson** (HHMI Janelia), TBA

09:45 AM - 10:30 AM **Adam H. Marblestone** (MIT), How Improvements in Neuroanatomy Could Shed Light on Cognitive Architecture

10:30 AM - 11:00 AM Coffee Break

11:00 AM - 11:45 AM **Jonathan B. Demb** (Yale University), Synaptic Mechanisms for Visual Computation in the Retina

11:45 AM - 12:30 PM **Marion Silies** (European Neuroscience Institute, Göttingen), Motion Vision: From Behavior to Cellular and Circuit Function

12:30 PM - 02:00 PM Lunch Break

02:00 PM - 02:45 PM **Anmo J. Kim** (Rockefeller University), Quantitative Predictions in a *Drosophila* Visuomotor Network

02:45 PM - 03:30 PM **M. Eugenia Chiappe** (Champalimaud Centre for the Unknown), An Internal Representation of Walking Movements in a Visual Area of the *Drosophila* Brain

03:30 PM - 04:00 PM Afternoon Break

04:00 PM - 04:45 PM **Katherine I. Nagel** (New York University), Neural Circuits Encoding Wind Direction in *Drosophila*

04:45 PM - 05:30 PM **Tim P. Vogels** (University of Oxford), TBA

Monday 9:00 AM - 9:45 AM

Circuits for Learning and Memory in the Adult Drosophila Mushroom Body

Gerald M. Rubin, HHMI Janelia Research Campus, Ashburn, VA.

The mushroom body (MB) is the major site of associative learning in insects. In the MB of adult Drosophila, each of 20 types of dopaminergic neurons (DANs) innervates distinct small compartmental regions of the mushroom body (MB). Different subsets of these DANs signal punishment and reward. We have recently shown (Aso & Rubin, eLife 2016) that these DANs appear to be able to write parallel memories in different MB compartments using distinct learning rules. I will discuss our ongoing efforts to explore the rules for writing, forgetting and updating memories in each compartment.

I will also present recent work done with the FlyEM Project Team at Janelia to determine the connectome of the three compartments of the vertical (or lobe) of the MB. The unprecedented level of detail of this dataset should enable modeling studies not previously possible and suggests many experiments to explore the physiological and behavioral significance of the circuit motifs we observed. That many of these motifs were not anticipated by over thirty years of extensive anatomical, experimental and theoretical studies on the role of the insect MB argues strongly for the value of electron microscopic connectomics studies.

Monday 9:45 AM - 10:30 AM

Long-Term Memory Requires Sequential Protein Synthesis in Discrete Mushroom Body Output Neurons in Drosophila

Ann-Shyn Chiang, National Tsing Hua University, Hsinchu, Taiwan.

Creating long-term memory (LTM) requires new proteins to stabilize learning-induced synaptic changes in the brains. In the fruit flies, Drosophila melanogaster, aversive olfactory learning forms several phases of memory to associate an odor with coincident punishment in sparse Kenyon cells within the mushroom body (MB). How brain circuits translate early phases of labile memory into long-lasting stable memory remains unclear. Here, we show that learning-induced new proteins for aversive olfactory LTM occur at discrete MB output neurons (MBONs). Acutely blocking protein synthesis with a temperature-sensitive ribosomal toxin, we found that LTM formation requires sequential new proteins in three subsets of MBONs at different time windows after learning. RNAi-mediated down-regulation of oo18 RNA-binding proteins (ORB) in any of these MBONs impaired LTM. Neurotransmission outputs from these MBONs are required during specific time windows after learning and essential during LTM retrieval. Together, these results suggest a LTM formation model that early labile memory encoded in neural activities of sparse Kenyon cells consolidates into stable LTM at discrete postsynaptic MBONs by sequential ORBregulated local protein synthesis at active synapses.

Joint work with Jie-Kai Wu, Chu-Yi Tai, Kuang-Lin Feng, Shiu-Ling Chen and Chun-Chao Chen.

Monday 11:00 AM - 11:45 AM

Brain Circuit Maps of Larval Drosophila

Albert Cardona, HHMI Janelia Research Campus, Ashburn, VA.

The projection neurons of the olfactory, gustatory, visual and temperature-sensing systems of the insect relay inputs to both the mushroom body and the lateral horn. While quite a bit is known about the nature of the inputs, little is known about the circuits of these two brain centers and how they relate to each other. To address this, we have mapped the wiring diagram of these two centers using electron microscopy-based neuron reconstructions. I will show how multiple sensory modalities are integrated in the lateral horn and how this information is relayed to the mushroom bodies and beyond.

Monday 11:45 AM - 12:30 PM

The Larval Standard Brain of Drosophila: The Mushroom Body Learning and Memory Network

Andreas S. Thum, Department of Biology, University of Konstanz.

Brains organize behavior. This involves the integration of present sensory input, past experience, and options for future behavior. The insect mushroom body is a paradigmatic case of a central brain structure bringing about such triadic integration. We use larval Drosophila to systematically study these processes at single-cell resolution. Our focus is bipartite as it includes research on the anatomical and behavioral architecture of the larval mushroom body circuit. On the anatomical level we use serial electron microscopy (EM) to reconstruct a synapse-resolution map (connectome) of the complete MB wiring diagram in a Drosophila larva consisting per hemisphere of about 110 KCs and exactly 24 mushroom body output neurons, 7 dopaminergic input neurons, 2 paired and 2 unpaired octopaminergic input neurons, 5 additional mushroom body modulatory input neurons, and an additional GABAergic feedback neuron. In addition, we study these mushroom body function with respect to appetitive olfactory learning at single-cell resolution, focusing on the behavioral architecture of the mushroom body input and output neurons, as well as the mushroom body intrinsic APL neuron. Ultimately, this data is then integrated in a newly established standard atlas for the larval brain, a five-part approach that includes the generation of an image registration framework, the generation of a larval standard brain, the segmentation and denomination of identified brain structures, the registration of several thousand Gal4 stocks onto the standard brain, and the organization of the obtained information in a web-based open access database called brainbase. Taken together this work provides a rich picture on multiple levels of how an insect central brain structure is anatomically and functionally organized.

Monday 2:00 PM - 2:45 PM

Parallel Olfactory Coding Mechanisms in the Drosophila Brain

Silke Sachse, Max Planck Institute for Chemical Ecology, Jena.

Animals use sensory systems to navigate the environment in a way that optimizes their survival and reproduction. The olfactory system plays here a major role in encoding chemical information and translating the outside world into a neuronal representation that enables an animal to take odorguided decisions. The vinegar fly represents a premier model system for studying olfactory processing mechanisms since it exhibits a stereotyped architecture which is similar to its mammalian counterpart, but is less complex and highly tractable as well as susceptible to genetic manipulations. By exploiting these genetic techniques and linking them to neurophysiological, molecular and behavioral methods, we are dissecting the neural circuits underlying olfactory coding and processing in the context of odor-guided behavior in Drosophila.

In order to understand higher odor processing we are scrutinizing the lateral horn (LH) of the protocerebrum, a brain region that is assumed to be involved in innate behavior. Two populations of projection neurons excitatory (ePNs) and inhibitory (iPNs) convey the odor information from the antennal lobe to the LH. We analyzed how different odor features such as hedonic valence and intensity are functionally integrated in this brain area. We could previously demonstrate that the LH can be classified into three functional odor response domains that decode opposing hedonic valences and odor intensity that derive from iPNs and third-order neurons that further innervate the ventro-lateral protocerebum. To investigate whether ePNs accomplish a comparable categorization of odor features and whether iPNs and ePNs interact, we have elucidated the neuronal circuitry of the two PN populations at a morphological and functional level. The talk will summarize our recent insights into the processing strategies of the two parallel output pathways to the higher brain and their contribution to odor perception.

Monday 2:45 PM - 3:30 PM

Understanding the Function and Specificity of Feedforward and Feedback Signals in Olfaction

Dinu Florin Albeanu, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.

Areas at the sensory periphery send feedforward signals to the cortex and, in turn, receive massive top-down cortical feedback. To date, the function and degree of specificity of such feedforward and feedback loops remain poorly understood. In the mammalian olfactory system, the bulb (OB) output neurons, the mitral and tufted (M/T) cells differ in their intrinsic properties and local connectivity, and project in a disjointed fashion to several areas including the piriform cortex (PC) and anterior olfactory nucleus (AON). In turn, both AON and PC send massive glutamatergic projections to local inhibitory OB interneurons (mainly granule cells, GC). To understand the logic of feedforward and feedback signals, we used multiphoton calcium imaging (GCaMP) and monitored the odor responses of M/T and GC cells in awake, head-fixed mice. We investigated whether mitral and tufted cells code odor identity and concentration differentially, and found substantial differences in their concentration response curve shapes, odor correlation patterns and dimensionality of responses. The cross-validated linear decoding performance for concentration-invariant odor identity was significantly better for the tufted versus the mitral cells population, suggesting distinct roles for these output channels in processing of olfactory information. Furthermore, we find that top-down feedback from higher olfactory brain areas depends on the functional type of feedforward input, and differentially impacts each of the two classes of OB outputs. We are currently investigating whether distinct sets of GCs synapsing on mitral vs. tufted cells are differentially modulated by feedback originating in the APC and AON. We propose that two neuronal circuits supported by the mitral and respectively tufted cells, their target brain areas and specific feedback signals, serve distinct computations in olfaction.

Monday 4:00 PM - 4:45 PM

Cracking the Olfactory Code

Vijay Balasubramanian, Department of Physics, University of Pennsylvania.

Monday 4:45 PM - 5:45 PM

Deep Learning and the Unknown Unknowns of Neuroscience

Konrad P. Kording, Feinberg School of Medicine, Northwestern University.

I will highlight fundamental problems in neuroscience using both computational and experimental arguments. I will use this as a backdrop to discuss how neuroscience can be informed by deep learning, highlighting various ways in which deep learning can inform neuroscience.

Tuesday 9:00 AM - 9:45 AM

TBA

Barry J. Dickson, HHMI Janelia Research Campus, Ashburn, VA.

Tuesday 9:45 AM - 10:30 AM

How Improvements in Neuroanatomy Could Shed Light on Cognitive Architecture

Adam H. Marblestone, Synthetic Neurobiology Group, MIT.

Neuroanatomy would benefit both from improved methods, and from computationally motivated theories that make distinctive predictions about mesoscale neural structures. I will describe an optical approach we are developing for high-throughput molecularly annotated connectomics, which treats long-range and short-range connections on an equal footing (a collaborative project among the Church, Boyden and Zador labs), introduce a theory of symbolic processing in the thalamo-cortico-striatal system (work with Ken Hayworth), and suggest how the former might in the future shed light on the latter. More generally, I will suggest neuroanatomical questions that could illuminate connections between biological brains and the kinds of structured architectures that are now finding use in deep learning.

Tuesday 11:00 AM - 11:45 AM

Synaptic Mechanisms for Visual Computation in the Retina

Jonathan B. Demb, Yale School of Medicine.

Information processing in a sensory system depends on the selective convergence of excitatory and inhibitory pathways in neural circuitry as well as activity-dependent changes in synaptic release. The first stage of visual processing occurs in the retina, where circuits are formed by specific excitatory and inhibitory interneuron types that selectively converge onto 40 types of ganglion cell, the output neurons that form the optic nerve. Ganglion cells adapt in order to operate under variable lighting conditions. Adaptation to both the mean light level and the variance around the mean, or the contrast, occurs beyond the photoreceptors within retinal circuitry. I will describe recent experiments that investigate mechanisms for adaptation in the circuitry of the mouse retina using receptive field measurements, optogenetic studies of specific synapses and computational modeling. Mechanisms for contrast adaptation depend on both synaptic mechanisms, including vesicle depletion, and network mechanisms, including lateral inhibition. Contrast adaptation in ganglion cell excitatory inputs can be explained by a divisive suppression computation that also contributes to millisecond precision of spike firing.

Tuesday 11:45 AM - 12:30 PM

Motion Vision: From Behavior to Cellular and Circuit Function

Marion Silies, European Neuroscience Institute, Göttingen.

Many animals use visual motion cues to navigate through the environment, find prey or escape predators. Long-standing theoretical models have made predictions about the computations that compare light signals across space and time to detect motion. Over the past years, core circuits that can implement such motion computations in Drosophila have been proposed based on connectomic and physiological studies. In the fly visual system, separate ON and OFF pathway exist that are specialized to detect the movement of light or dark edges. These pathways already split downstream of photoreceptors in the lamina, where L1 and L2 provide the major inputs to the ON and OFF pathway, respectively.

Using forward genetic approaches, we identified neurons of a third visual pathway in which the first order interneurons L3 provides a key input to direction-selective neurons via the medulla neuron Tm9. Neurons of this pathway are behaviorally required for OFF motion detection and form a novel, parallel OFF pathway. Using in vivo two photon calcium imaging, we showed that this pathway carries sustained responses to contrast changes and exhibits receptive field properties that inform elementary motion detectors about wide regions of visual space. Thus, the two OFF pathways differ in their physiological properties and the first order interneurons L2 and L3 already provide fast and slow inputs to OFF edge motion detection. We are currently investigating the mechanisms that shape the distinct properties of the OFF pathway. Our goal is to understand the cellular mechanisms, circuits and computations that implement behavioral responses to visual motion.

Tuesday 2:00 PM - 2:45 PM

Quantitative Predictions in a Drosophila Visuomotor Network

Anmo J. Kim, Rockefeller University, New York.

Vision influences behavior, but ongoing behavior also modulates vision from insects to primates. For example, we constantly move our eyes from one point to another, even as we view a static scene. These eye movements cause the whole visual image to shift on our retinas; yet we hardly notice they are happening. The same visual motion, if replayed, causes a strong sense of visual motion. Consistent with this behavioral observation, previous studies reported transient modulation of visual processing during rapid eye movements. However, the function and biophysical mechanisms of most such modulations remain unresolved. We investigated a function for behavioral modulations of visual processing in Drosophila by combining behavioral genetics, electrophysiology, and high-speed videography. We provide evidence that, via a genetic inactivation experiments, a set of motion-sensitive visual neurons regulate gaze-stabilizing head movements. We describe how, during flight turns, Drosophila perform a set of head movements that require silencing their gaze-stability reflexes along the primary rotation axis of the turn. Consistent with this behavioral requirement, we find pervasive motor-related inputs to the visual neurons, which quantitatively silence their predicted visual responses to rotations around the relevant axis while preserving sensitivity around other axes. This work proposes a function for a behavioral modulation of visual processing and illustrates how the brain can remove one sensory signal from a circuit carrying multiple related signals.

Tuesday 2:45 PM - 3:30 PM

An Internal Representation of Walking Movements in a Visual Area of the Drosophila Brain

M. Eugenia Chiappe, Champalimaud Centre for the Unknown, Lisbon.

Animals move their body in specific, coordinated, and flexible ways during locomotion, and this high-performance control depends on an internal estimate of self-movement. Self-movement estimation is also critical for the proper interpretation of external sensory information that may guide locomotive behaviors. This internal representation is thought to arise from the distributed activity of sensorimotor circuits; however, it is still unclear what circuits are involved, and how they implement motor-sensory coordination. Here we will discuss our initial attempts to uncover these issues in Drosophila melanogaster by performing simultaneous recordings of the flys walking behavior and the activity of a group of optic-flow processing neurons, the HS cells. Our results show that HS cells encode information about the flys walking movements in darkness, suggesting the presence of extra-retinal signals in this network. HS cells show direction selective responses driven by the turning direction of the fly, which cooperate with the cells canonical (visual) direction selectivity under visual stimulation. We propose that the observed convergence between visual and motor-related information during walking in HS cells creates a non-ambiguous, quantitative central representation of the movement of the body through space. This accurate representation may guide the flys forward movements during explorative walking. Ongoing experiments in Virtual Worlds for freely walking flies are testing this functional hypothesis.

Tuesday 4:00 PM - 4:45 PM

Neural Circuits Encoding Wind Direction in Drosophila

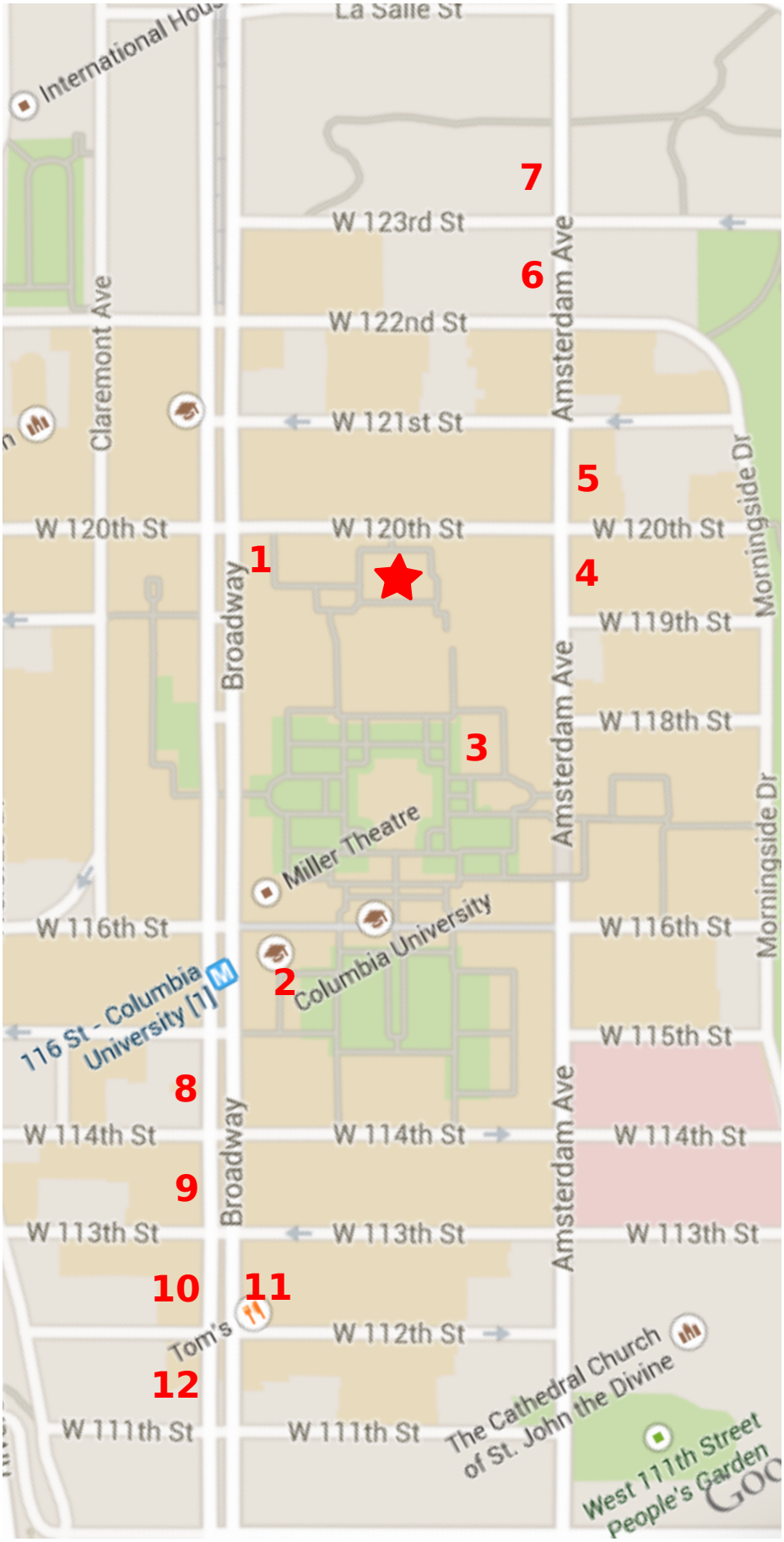
Katherine I. Nagel, NYU School of Medicine.

Wind direction is an important cue for navigation in many insect species. Drosophila are known to detect wind direction using antennal mechanoreceptors (Yorozu et al., 2009) but the central circuits downstream of these mechanoreceptors are not known. Using a novel behavioral paradigm, we show that walking flies use wind information derived from antennal mechanoreceptors to guide olfactory navigation behavior. Next, we use whole cell recordings to identify central neurons downstream of the antennae that encode wind direction information. We show that two groups of putative second-order neurons encode motion of the ipsilateral antenna, and have opposing direction tuning. We further identify a group of putative third-order neurons that exhibit strong directional tuning for wind stimuli. These neurons project both ispilaterally and contralaterally, where single-cell fills suggest they contact their sister cells in the opposite hemisphere. Antennal manipulations demonstrate that these neurons combine information from the two antennae nonlinearly to increase the dynamic range and discriminability of wind direction signals. Our findings suggest an ascending wind pathway that extracts wind direction information from positional signals derived from the two antennae.

Tuesday 4:45 PM - 5:30 PM

TBA

Tim P. Vogels, Department of Physiology, Anatomy and Genetics, University of Oxford.



Workshop Venue

On Campus

1.
Joe Coffee at Columbia (2nd floor)
W. 120th St & Broadway

2.
Brad's Brew (coffee brew and sandwiches)

3.
Brownie's Cafe
In basement of Avery Building (School of Architecture)

Block 4. Time by Foot: 2 mins

Che Bella Pizza (Italian)
1215 Amsterdam Ave

Subsconscious (Submarine Sandwiches)
1213 Amsterdam Ave btwn 119th and 120th Sts

Amsterdam Rest. and Tapas Lounge (Continental)
1207 Amsterdam Ave btwn 119th and 120th Sts

Block 5. Time by Foot: 2 mins

Appletree Deli (Sandwiches and Deli)
1225 Amsterdam Ave btwn 120th and 121st Sts

Panino D'Parma (Italian Deli)
1231 Amsterdam Ave btwn 120th and 121st Sts

Ajanta (Indian)
1237 Amsterdam Ave btwn 120th and 121st Sts

Massawa (Ethiopian)
1239 Amsterdam Ave at 121st St

Block 6. Time by Foot: 4 mins

Kitchenette (American)
1272 Amsterdam Ave btwn 121st and 122nd Sts

Subway
1270 Amsterdam Ave btwn 121st and 122nd Sts

Maxx Cafe (Italian)
1262 Amsterdam Ave btwn 121st and 122nd Sts

Block 7. Time by Foot: 5 mins

Nikko (Asian Fusion)
1280 Amsterdam Ave at 123rd St

West Place (Chinese)
1288 Amsterdam Ave btwn 123rd and La Salle Sts

Block 8. Time by Foot: 7 mins

Starbucks

Block 9. Time by Foot: 8 mins

Bernheim and Schwartz
2911 Broadway btwn 112th and 113th Sts

Block 10. Time by Foot: 10 mins

The Mill Korean Restaurant (Korean)
2895 Broadway btwn 112th and 113th Sts

Community Food & Juice
2893 Broadway btwn 112nd and 113th Sts

Le Monde (French / Brasserie)
2885 Broadway btwn 112th and 113th Sts

Block 11. Time by Foot: 10 mins

Tom's Restaurant Diner
2880 Broadway at 112th St

Amigos (Mexican)
2888 Broadway btwn 112th and 113th Sts

Deluxe Diner (American)
2896 Broadway btwn 112th and 113th Sts

Block 12. Time by Foot: 11 mins

Chipotle Mexican Grill
2843 Broadway btwn 110th and 111th Sts