Mar 1-2, 2022 – BBQ Workshop – Day 1 – Transcript

Speaker 8: Great. Well, we have hit the one o'clock hour. I want to say thank you to everybody that has joined today for what I think is going to be very exciting and fruitful workshop that bring behavior, quantification, and synchronization workshop. This workshop will be a little different and very heavy on discussion, so we're really excited about having everybody to give their questions and having a very fruitful discussion. With that, I'm going to turn this over to our first speaker, Dr. Holly Lisenby from the National Institute for Mental Health.

Dr. Holly Lisenby: Thank you Dana, and welcome everyone to the Brain Initiative supported workshop on brain behavior quantification and synchronization. I'd like to thank you all for joining us for what we expect is going to be a really exciting and fun our next two days. My role is to set the stage and describe the goals of this workshop. Why is Brain Initiative supporting a workshop on brain behavior quantification and synchronization? The rationale is outlined here. Basically, behavior is the primary output of the brain. To really understand the neural origins of behavior, it's really essential to our goal of advancing neuroscience and ultimately using that science to support brain health. But this is a complex challenge because understanding behavior in its full complexity requires a detailed and multidimensional analysis of a broad range of behaviors in a context of environment and interaction with the environment. Now, our tools for quantifying the brain side of this equation are really quite advanced and are getting even more advanced through Brain Initiative investments. We've got great tools now for quantifying neural activity with very high temporal and spatial resolution. But on the behavior side, typically we're measuring behavior at lower resolution. This can make the discovery of causal linkages between brain and behavior challenging. Indeed, the tools for measuring the full richness of species' appropriate behaviors in environments and synchronizing these with simultaneously recorded neural activity are presently lacking. This research gap was not lost on the brain 2.0 report, which specifically called for more sophisticated methods of quantifying behavioral, environmental, and internal state influences on individuals. Thus, our topic for today's workshop; Brain Behavior Quantification and Synchronization. On this slide, I'm going to map out a conceptual terrain about what we currently have in the black font, what we have, but could be improved in the purple, and what we don't have, which are the research gaps in red. Starting on the brain side, we currently have high temporal and spatial resolution tools for measuring and quantifying neural activity. On the behavior side, especially in a laboratory setting, we do have great tools with good resolution for studying behavior. But typically, we're standing behaviors that are not naturalistic. The measurements often fail to capture the full range of behavior and often fail to capture the environment that the subject's interacting with. We do currently have tools for linking neural activity recorded simultaneously with behavior in the lab. But as you'll see, typically, these tools require bulky equipment. It limits the movement of the subject, and when we're trying to model these data that are mismatched in terms of their temporal resolution between the neural side and the behavior side, this poses challenges for modeling as well. Now, we do already have tools that allow us to take experiments into naturalistic settings and capture behaviors that are ecologically valid in the real world. But our current tools typically have only a few channels of recording and limits in terms of the range of modalities that can be simultaneously sampled. Now, in red here is a big research gap. We're presently lacking practical systems that allow us to bring neurocircuit recording into the real-world setting so that we can capture what the brain is doing when it's generating these behaviors in the real-world. Now, I've illustrated here as a cloud, this thing that's difficult to get a handle on, objectively speaking, which is internal subjective states. We currently lack direct objective measures of these. Often we're limited to self-report of the subject telling us what they're experiencing or proxy behaviors that we think are related to the internal state. Now this is an important gap because many of these internal states are topics of specific clinical interests such as intention, craving, mood, thought, hunger, perception, pain, reward, suicidal intent. These are things that we would really like to be able to objectively study. In the absence of objective measures of these, we are currently lacking a reliable way of training decoders that could use neural activity to inform us about these internal states. Without these, this has been an impediment for the development of interventions as well. Here's some examples of state of the art technologies that are currently being used in research. This, for example, is a wearable recording of intracerebral EEG in subjects who were freely navigating a space. You can see that as a subject is walking around this room, the cameras on the ceiling and the tracker on his head is able to track where in space he's located. To do this simultaneously with brain recordings on the right part of the slide, this setup was able to demonstrate that when the subject himself was navigating the room, a specific neural signature is seen, which is quite different than when he's watching someone else navigate the room, thereby really illustrating the importance of the environment, what's going on around the subject. Now, as powerful as this tool is, it's still lacking in some ways; it's only measuring one aspect of behavioral response, it has limited capture of the environment and sensory cues that the subject is responding to, it's limited to the laboratory environment, and look at the backpack he's wearing, it's really bulky equipment and head mounted gear, and it only tracks where he is in space, not his actual body movements or postures. This turns out we actually already have software platforms such as dance illustrated here, which are able to use deep learning to derive measures of naturalistic behavioral repertoire without having to put markers on a subject. This is a very exciting opportunity to discover the neural basis of these naturalistic behaviors. But still, it's lacking the full range of behavioral response and it lacks capture of the environment and sensory cues that may be influencing the behavior that's being measured. Now, let's go back to this conceptual map. If we could take these research gaps and turn them into opportunities, what would it mean for neuroscience if we could do that? For example, if we could have an expanded array of sensors to capture the full range of behavior in the environment and in the lab and link these at the same temporal resolution with simultaneously recorded neural activity. What if we could deploy next-generation sensors or existing sensors that are not currently being used in neuroscience? Deploy these in real-world settings to inobtrusively record naturalistic behaviors and environments. What if we could develop portable tools for neural recording in real time, in ambulatory settings to be able to link these naturalistically recorded behaviors with what the brain is doing at the time that it's generating those behaviors in those natural environments? We might have then the potential to use these high dimensionality data streams to have more accuracy in our ability to infer internal states from these quantified behaviors. If this could give us a more objective means of inferring internal states and interests like mood disorder or suicidal intent, this then gives us the opportunity to tag neuronal activity simultaneously recorded during internal states of interests to begin to be able to decode these internal states from the neural activity themselves. If we had that, then we might be able to build closed-loop systems that would be able to modulate neural activity with behavior actually in the loop. Now why do we think the time is right to have this discussion? We are currently experiencing explosion of new and advanced inobtrusive, stationary, and wearable sensor technologies, platforms to integrate multimodal data, to use advanced tools of data science to make sense of these data and to package this in a way that allows data visualization and analysis. There's a lot of new developments that have not yet been exploited for neuroscience applications. This gives us the potential to use next-generation sensors, such as for self-driving cars to help us meet unmet needs in brain health. Now, talking about data, we know that internal states can generate a kaleidoscope of different types of behaviors that can be measured using a variety of arrays of sensors like videography, ultrasound, chemosensory, PISA sensors, and thermal sensors. That would generate high dimensionality data. That's an opportunity for data-driven modeling, theory building and testing. This type of approach could be synergistic with the Brain Initiative investments in informatics, in the development of new data archives, data standards, data integration approaches, software development, and secondary data analysis. Speaking of informatics, we have an opportunity to leverage existing multimodal data archives such as neural data without borders and the distributor archives for neurophysiology data integration, which already accepts behavioral data streams. We had the opportunity to build on already existing data standards that Brain Initiative has invested in for the cataloging behavioral data and standardizing the way we define behavioral tasks such as behavioral test description language. It's an opportunity to expand on the brain informatics portfolio by developing data archive standards and software tools that are currently lacking, specifically for cross-modal data fusion that incorporates information about the environment as well. We have an opportunity to generate a common data ecosystem across these data streams with pathways for dissemination. Here's an example of proof of concept of what a brain behavior quantification synchronization project might look like. We're going to be hearing more from Dr. Provenza later in this workshop. The goal here was to train an adaptive deep brain stimulation system for the treatment of obsessive-compulsive disorder. It starts with doing simultaneous neural recordings while different behaviors are being sensed, both in the clinic as well as at home and to be able to have this high temporal resolution linkage between what the brain is doing when it's generating the behaviors in these different contexts, and to really put behavior in the loop to train this adaptive DBS system. Here's an example of the type of data streams that can be captured with this type of approach. We've got computer vision to capture micro movements of the face, and then for [inaudible 00:56:52] we've got autonomic recording, we have EEG, and then you can increment the DBS amplitude and see how the behaviors respond. With this enriched multimodal data stream, it gives us the opportunity to begin to infer internal states from these quantified behaviors and then use that information to train adapted DBS systems that would be able to modulate state and disrupt the maladaptive behaviors when and where they occur. This brings us to the concept of brain-behavior quantification in synchronization and we publish this concept. The goals of which are to develop high-resolution tools and platforms to precisely quantify behavior as a multi-dimensional response to environment and interaction with environment with high resolution and to synchronize this information with simultaneously recorded brain activity. Another goal is to use this data and these tools to build new conceptual and computational models, so behavioral systems, and then use those models to test causal relationships between brain and behavior. Another goal is to establish a cross-disciplinary consortium to develop and disseminate these new tools, these ontologies, these research designs, and importantly, ethical frameworks that could have the potential of transforming how mechanistic brain behavior research is conducted. The establishment of the consortium across disciplinary is part of the goal for our workshop today. Our envisioned impact of this concept could be the dissemination of new technologies to transform how we go about understanding how the brain generates behavior, the development of new paradigms to establish causal relationships between neural activity and behavior. Ultimately, this could enable the development of therapeutic interventions for complex neural behavioral disorders that currently lack treatments. We'd also like to see a robust ethical framework that addresses the implications of using these tools to capture and record a person's experience. Now, there are two case examples I'm going to walk through, and then I'm going to introduce the format of our workshop today. The first use case example is when the behavior is the target of study. This is the most obvious use case situation, but we might need new tools to discover the neural basis of this behavior, which might be challenging to study for a number of reasons. It might be that the behavior only occurs in a real-world setting outside the lab, or could be the behavior occurs too infrequently to be captured in a lab, therefore, it requires ambulatory monitoring to capture, or it could be that the frequency at which the behavior occurs over extended periods of time is itself salient, such as in the case of seizures or binge eating. Here's an example of applying computer vision to capture and quantify a naturalistic behavior. In this case, spontaneous fly behavior, but the concept would be to do this across different species and different settings. The potential impact could be advancing our understanding of how the brain generates these complex behaviors in particular complex environments, and also enabling the development of interventions whether they're closed-loop or otherwise, when the behavior itself is the targeted therapy. But what about a different use case scenario? What if it's not the behavior that's the target, but it's the internal state that's the target of study? In this case, behaviors are being used as markers of internal subjective experience that cannot be measured directly like a thought process in our affective state or a perception. Here the subjective experience for which the objectively measured behaviors serve as a marker is the intended target of the study, not the behaviors themselves. Here's an example of using computer vision again, to quantify dynamic micro-movements of the face over time and then use these to infer internal affective state. Ultimately, this type of technology could be linked with simultaneous neural recording and stimulation as you'll see from some of our speakers in the workshop. The potential impact here could be to advance our understanding at how the brain generates subjective experiences and ultimately could enable the development of interventions when the subjective experience is the therapeutic target. Now, the goals of this workshop. Are to convene a diverse panel of experts from a variety of fields that maybe don't often talk to each other. We've got neuroscientists, data scientists, sensory developers, behavioral experts, engineers, ethicists. We've asked them to engage in cross-disciplinary dialogue to stimulate the creation of new paradigms to study behavior. We've asked them to help us highlight where opportunities are, where research could make the most impact, we've asked them to identify where the needs are, where new technology needs to be developed. We hope that this will be the start of the formation of consortia to stimulate progress in developing new behavioral ontologies, technologies, informatics, computational tools, and ethical frameworks. I'm going to give you a bird's-eye view of what is to come over the next two days. We start with a panel on behavior as a complex system within a complex system. The panel's comprised of speakers and discussants and it has a moderator. In this first panel, we've formatted a conceptual data blitz or conceptual blitz, where we've asked the speakers and discussants to think through, how do we frame our research questions to study behavior as a complex dynamic system in interaction with a complex environment. Our second panel will be on sensing behavior in its environments, the dimensions, and dynamics of this. Again, we've got four speakers and three discussants, and we've asked them to think about how do we capture the information needed from individual organisms, social groups, and physical environments that we need to capture the complexity of behavior, particularly in real-world settings. Then our third panel will be on what are the computational opportunities and challenges from modeling brain behavior environment as a complex dynamic system. Then closing out day 1, we've asked Karen Rommelfanger and Justin Baker to provide some synthesis and closing remarks from the three panels across day 1 and to highlight for us where the opportunities and challenges may lay. Then day 2 is going to start out with three really exciting talks, which will integrate the concepts from day 1 to advanced neuroscience. We have Murphy [inaudible 01:03:41]. You can see the topics of their talk shown there. After the three talks, we're going to have concurrent moderating breakout sessions. The first one is, I'll be moderating on human and clinical research along with our breakout colleagues, [inaudible 01:04:00] and Katherine Scangos, and then the simultaneous breakout will be on organismal prepared of research moderated by a Patrick Abbott from NSF, and we have Phil Hook and [inaudible 01:04:13] will be our discussants there. If you can't decide which breakout to attend, don't worry. They're both going to be recorded and they'll both be streamed after the meeting. Then, of course, we're really excited to be welcoming Dr. John Ngai, who is the director of the NIH Brain Initiative to give our closing remarks and synthesis after we have the report out from the groups and discussion. It's going to be a really exciting two days and we're going to be looking forward to hearing from our breakout groups what are the high priority areas of research to pursue? What are the tools needed to pursue them? What are the barriers that we need to address? There's so many people to thank and listed the planning committee and members who helped to organize this meeting on this slide here, and as you can see, this is a collaboration across multiple NIH institutes and offices as well as NSF. Now, to set us up for panel 1, which is going to be on behavior as a complex system within a complex system, we're going to have 48-minute talks followed by discussion. Each discussant will introduce an idea or question generated by the talks and then lead a discussion for about nine minutes. Then they'll handoff to the next discussion. Workshop participants are invited to use the chat to post questions for the discussion and other attendees, please use the Q&A box or live feedback functions in Zoom or Video cast. Now, without further ado, I'd like to introduce Dr. Jeanine Simmons, who's our moderator for panel 1.

Dr. Jeanine Simmons: Thanks, Holly. I'm excited to be launching off panel 1, I think, [inaudible 01:05:50] workshop for years, so I'm super excited. The panel 1, as Holly said, is entitled behavior as a conflict system within a complex system. Questions here are, how do we frame our research questions to study behavior as a complex dynamic system. The speakers are Iain

Couzin, Jeffrey Cohn, Nicole Provenza and Lena Ting. Then our discussants will be Molly Cummings, Timothy Wright and Ben [inaudible 01:06:18]. I will now turn it over to Ian.

Iain Couzin: Hi, everybody. I have to apologize, my family's had COVID last week and I thought I was going to escape somehow unharmed. But I started having some rebound symptoms today and I tested positive. So please excuse the voice and coughing, and fatigue, and so on. I just couldn't miss this amazing event. I was tricked by behavior as a complex system within a complex system. Because I think that neuroscience, of course, is developed these incredible tools that we just heard about that span across these thirsts spatial and also temporal scale. Now I love this piece by [inaudible 01:07:09] tomorrow because [inaudible 01:07:12] extends to evolution rescales. The behavior doesn't make sense if we don't consider how these scales feedback on each other. Multiscale imaging has been so critical for neuroscience. Animal behavior, I think one of the wonderful challenges is that it inherently spans both temporal and spatial scales. Animals need to respond at a sub-second scale to a risk or a threat. They have to respond by the minutes in terms of food resources, they have to respond potentially over the years, in terms of with whom they choose to mate. There are many feedback processes across the scales. They can't be decoupled in a simple way. Like who you choose to mate with actually impacts many aspects of your life. We've already seen this, I didn't see the previous talks just coincidence for this wonderful work from Timothy Dan. But this is characterizing the whole body of work led by the metaphysis, Gordon Berman and others to try to develop quantitative tools to study and to describe stereotypical behaviors. I think this has been absolutely transformative to the whole field of behavior. In fact, I think behavior is really undergoing a renaissance. When I was a postdoc at Oxford University we thought behavior was monitored. We did it all in the 70s and 80s because mechanism was never a focus. Now we're realizing that mechanism is fundamental to understanding how the brain processes information. But yet we're still only at the very beginning of our studies. I think that's the exciting thing. Instead of talking about my own work today, I wanted to really talk about what I've been thinking about certain late last night when I was preparing my slides. About what are the major challenges and gaps in the study of behavior? Some of this will reflect what you just heard because I think independently thinking the same types of things. We're getting pretty good at doing posture analysis as we just saw on describing stereotypical patterns from high-dimensional postural data. What we're not so good at doing at the moment, I would love to hear more about this from the other participants, is how animals taken high dimensional sensory information, usually multimodal acoustics vision, and other sensory modalities. The brain of course, is this wonderful dimensionality reduction entity that allows animals to make sense of this, to make decisions based on memory and physiological states in genetics. As was mentioned before, behavior can actually give us insights even into these internal states. But we still really lack this formal way using say informational theoretic tools to actually allow us to causality. Correlation, yes, but causality is still very challenging and one of the reasons, and I'll come back to this, is that we have these recursive feedbacks across multiple timescales. I think that's a very important aspect that will improve all of our research. Another aspect I become very interested in, I think is a weak link so to speak. It's often movement is considered as the outcome of the seasons. That I don't know besides what it wants to do or that moves to get to the location it wants. But an actual fact, the movement isn't an icon of decision-making. We've been finding inherently a dynamical feedback between motion-sensing and decision-making and others. But this is yet a very small fields embodied decision-making. I think it's very important to consider the brain is embodied in the organism. In order to explain and understand spatiotemporal computation. Maybe I was in the audience that he's done some wonderful work that shows this too. I don't have time I don't want to talk about my research, but I do want to emphasize that have been really looking into this in a comprehensive way with a range of different systems and showing that we simply cannot make sense of the decisions animals make when I including this recursive feedback. This reveals that the brain is behaving as a dynamical system with processes like bifurcations, that breakup this complexity of the world into a series of binary decisions. I think this could integrate very well with classical neuroscience in terms of two options decision-making because we find that the brain spontaneously changes the world no matter how many options there are into a series of two option decisions and we compare that theory with experiments. Another aspect is that no animal is an island. Social behavior has been truly described and truly self-considered I guess within this type of framework. But almost all decisions any animals make involves either indirect or direct social information. Looking at classic models, the models that we can use in our community and in our entity works on this. C. elegans is a highly social animal so the social digging, odor avoidance is collected. They also use social information to forage, to choose mates, and so on. But those organisms just often and feel incredibly hard to study in a natural environment. Now, I think we have at least two model systems that would be perfect for crossing skills between natural environments and social complexity and controlled experiments zebrafish being one. They have territorial behavior that is ritualized fights with territories, schooling of course, rats. We were one of the first groups to ever ask this basic question, what happens if you put two rats memories or eight rats memories? Of course they solved this space collectively with some wonderful examples of how interactions can lead to cognitive abilities beyond the individual. I'm going to be a little bit a dramatic now or just push you a little bit, but I would argue that the behavior of these organisms, even these model organisms, is almost always studied in the absence of contexts in which it developed. By doing so, we severely restricts and also bias the behaviors that we studied. Also needed to limit the scope of our studies but it fundamentally it means we can least understand our data. But it becomes extremely hard to connect mechanism with new evolutionary processes, which is ultimately what matters if we do so. An example is collective migration. People put tags on individual animals and thought the individual was doing everything for themselves but almost all migrations and I learned to be collective. So why studying collective behavior particularly challenging? Well, it's very hard to determine cause of relationships and this is another area that we need to have developments in. Even if you have just two animals, one may be influencing the other strongly at one moment of time and not the other. But then when we think of a third animal is being influenced by A, or B influenced by A and C via the indirect effects. Of course, we can have more complex relationships. We've been trying to study this within schooling fish and flocking birds and it's extremely challenging to work at a cause of influence. Towards a solution I really excited by developing virtual reality environments, immersive holographic virtual reality, where individuals can interact freely within virtual worlds and we can network of our systems together. Here, you can see a virtual individual moving in a circle with the orange trajectory and the real separate is following it with a red trajectory it believes to be in the time with it even though this is an illusion based on the projection surface. We talked to more than one individual into these types of environments because we have to protect the world precisely from the perspective of the animal. But we can create multiple systems and network them together and then allow real individuals to interact with each other, not in the same physical world but in the same holographic world. This gives us great control to understand what's going on. We have now 11 of these systems here in constants and so here you can see four individuals who are not interacting in the real physical world but in a holographic world. Working with Amabile who recently moved to us from Harvard University, we connect this virtual environment also with the microscopes so we can do whole-brain imaging, cellular level resolution of animals freely interacting with each other in these other holographic environments in fact one of them could be in the US and yet the bandwidth is large enough that we could still have them interact. Also working with [inaudible 01:16:18], Harvard University will be looking at zebrafish as a model for autism spectrum disorder using 92 genes associated with these conditions to really understand how they're influencing sociology. But there's a massive gap in our studies of behavior. Almost all studies focus in controlled, smaller, overly simplistic laboratory environments. The so-called microscopic if you run back to the beginning of my talk or in the uncontrolled conditions of the world are microscopic and I'm involved in both communities, but very few people are. We have this beautiful work by Timothy and others at the microscopic scale. We've been doing so this is a paper that we've used the state of art technology in the wild to track animals as they migrate stocks as an engraving of Sub-Saharan Africa. But we have almost nothing in the middle. The microscopic scale is just, the void is a barren line and that means our communities don't reach each other, we don't talk to each other, we don't make these connections which is as important as anything else. Knowing this, when I built this new building in constants that has this large indoor facilities that will allow us to begin to address this. This is [inaudible 01:17:33] who worked with Carlos [inaudible 01:17:36] with the [inaudible 01:17:38] very recently and beyond the proof to illustrate where you have rats choosing between two different options thousands of times to allowing them to move within large environments while doing brain imaging. This is a 15 by 15 meter environment that allows us to do this. Also, this is another test where we can also do this type of work and also look at the acoustic communication. Thanks a lot. [inaudible 01:18:07]

Speaker 5: Dr. Cohn, can you turn on your video.

Dr. Jeffrey Cohn: Got it. Okay.

Speaker 5: Thank you.

Dr. Jeffrey Cohn: Good. I'm going to be talking about behavior in humans and how best to measure behavior for moral science. Commonly used to self-report and it has a number of advantages. It's convenient, it's fast, allows for quantification, it's easily obtained. There are many reliable questionnaires it shoots from. The disadvantage, of course, is that it requires the ability to speak, write, or gesture. That can't be done in young children. It can't be done in people who are on breathing tubes or who are communicationally challenged. It's idiosyncratic, the meaning of those measures vary with a person, and it's limited to what is consciously aware. It's susceptible to suggestion, impression, deception. This temporarily sparse. We can only get it when we ask a question and you can only ask so many questions in any period of time and it lacks analogs in other species. How else to measure behavior? Facial expression is one that we've been especially interested in. Face, head, and body move presents another. Voice quality and timing and then physiology, which can be measured either with thermal camera or context sensors. All of these modalities have been well-studied in people and in developmentally and culturally. My own approach has emphasized facial expression, and that's what I'll focus on today. Facial expression is made possible by a dense mesh of facial muscles. Unlike muscles anywhere else in the body, they connect to each other or they connect the soft tissue. This gives a high degrees of freedom for facial expression. The approach we use annotation is based on Ekman's Facial Action Coding System. In that system, each muscle or a small number of muscles, is referred to as an action unit and these have a high degree of control. We are interested in the occurrence, the intensity, and the timing of facial actions. With that system, we can track, change an expression and we can describe it in terms of these molecular movements. The approach that we use developed in collaboration with [inaudible 01:22:21] , Laszlo Jeni or [inaudible 01:22:26] is Automated Facial Action Recognition, which we refer to it as FR. What's showing on this slide is one version of the system. There are a number of versions that we've been using is a computer vision machine learning-based approach to measuring facial actions and head and face dynamics. It's been trained on large and heterogeneous data and it's generalizable to participants such as I'll be talking about with deep brain stimulation. In work with [inaudible 01:23:05] medicine, Wayne Goodman Nicole for that will be following me. We've been interested in the relation between stimulation of the ventral striatum nucleus comments of [inaudible 01:23:24] patients. There are five patients who are undergoing treatment with deep brain stimulation or treatment resistant obsessive compulsive disorder. One context is programming sessions in which the parameter settings of the device are adjusted in order to optimize sleep in this series of programming sessions over a period of months. The second context is interviews, clinical interviews over the same period of time for more naturalistic behavior. This slide shows an example from a programming session. Here you can see the DBS amplitude and over here we're tracking positive effect in head velocity. Note that there is a close coordination between changes expression of facial affect expressed in terms of the zygomatic major and orbicularis oculi contraction, represented by these action units, and as well as head velocity. In clinical interviews over the same period of time, we looked at the relation between facial ethic and head dynamics in relation to the DBS energy, which is a function of amplitude, pulse width, and frequency and found that close to 30 percent of the variance in DBS energy during an interview can be accounted for by head dynamics and facial action units. We looked as well at their relation to Y-BOCS tool severity scores, Y-BOCS tool is a measure of OCD severity. Here, head dynamics and facial action units accounted for about 20 percent of the variance, which is rather strong. I would say strong effect in this context. As an example of DBS in a clinical interview, we have two interviews. This is from a case study early on in one. This individual has the DBS is on and the second video shows DBS off after a period of about three hours. Note that there was a dramatic difference in his facial ethic during these two conditions. When it's on, there is intense positive affect cycling on and off, brow raises, smiles, and so on. Very little, very few indices of negative affect whereas when the DBS is off, you'll see dramatic increases in negative affect, and very little in positive. In conclusion, facial expression has revealed time-locked changes in neural activation and longitudinal variation in more naturalistic contexts in DBS and symptomatology. Facial expression is one of many modalities that can be applied in human and comparative studies of brain and behavior. Going forward, we're interested in expanding the number of neural sites. So far we've primarily been looking at sites associated with OCD. In a separate study with seniors chef, we're looking at depression and using the facilities of the epilepsy monitoring unit at Baylor in order to look at a larger number of sites in relation to their effect on or output in terms of facial ethic and head pose along with other modalities. These are some of the additional modalities, voice quality and timing, speech and sentiment, peripheral physiology and social interaction. We have two broad goals. One is behavioral biomarkers for adaptive deep brain stimulation. We call [inaudible 01:28:32] , we'll be talking more about that in the very next talk. More objective measurement of behavior in clinical trials. Currently, for clinical trials, the primary outcome measure is self-report. We want to use multi-modal measures to more objectively measure tautology and response to treatment and work with deliberate. We've been looking at predicting Hamilton depression scores and using multi-modal measures. So far encouraging results are accounting for about 60 percent of the variation between observed Hamilton scores and predictive last. In terms of challenges, we need more data. Data is the key for learning. One of the constraints, those constraints of clinical settings that were not set up as laboratories in an epilepsy monitoring unit, for instance. The lighting is hospital lighting. How do you improve that and how do you impact the environment in a way that facilitates improved measurement? A second aspect is synchronizing video and neural data. More generally, synchronizing multi-modal behavioral data and neural data. This is an area that is really in need of important advances. With that, I'd like to thank you for the opportunity to present today. Thank you.

Dr. Jeanine Simmons: Thank you very much. Hopefully, you can all hear me a little bit better now, we're moving to the third talk megacolon events, [inaudible 01:30:33]. Great. Thanks.

Nicole Provenza: Hi everyone. I'm Nicole Provenza, I'm a post-doc in doctor sooner South Slavic Baylor College of Medicine and obviously he on progress and next steps toward conducting human neuroscience and ecologically valid environments. I have no disclosures to report. There's a whole key challenges that I think needs to be addressed in order to link neural activity to behaviors underlying psychiatric disorders. One is symptom heterogeneity. Psychiatric diagnoses are lacking. They are essentially defined by clusters of symptoms and there's a lot of symptoms heterogeneity even within the same diagnosis. Next, symptoms are subjective. Even if we have an idea of the symptoms we want to measure, how are we going to measure them? This is really challenging in psychiatry as there are no established physical readouts of symptoms state, like in movement disorders. Clinician administered skills, as Dr. Cohen mentioned, are used to assess severity of psychiatric disorders and they depend on subjective input from the patient. Three is sparsity of behavioral information. These self-report scales are meant to be administered on about every two weeks and so if we administer them more often, say every day we don't have a metric for every moment of every day still. These self-report skills are temporally sparse compared to our densely sample of neural data. For my work, I'm motivated to overcome these challenges, to identify biomarkers that can be used in an adaptive deep brain stimulation system to improve outcomes of DBS in severe OCD and depression. This work is part of an NIH QE3 effort led by Dr. Wayne Goodman. What this would look like is we would record neural signals continuously from the brain, use those signals to classify irrelevant brain states such as an obsessive-compulsive symptoms state, and then control stimulation parameters accordingly to relieve symptoms. Identification of irrelevant behavioral state and the brain state underlying this behavior is really critical for achieving this goal. One of the many strategies toward finding a neural biomarker would be to try to relate your old features, some more densely measured behavioral features. In my previous work, we did this with OCD participants implanted with sensing capable of DBS devices and the ventral capsule, ventral striatum region. We measure behavior during concurrent neural recordings both in the clinic and at home. In the clinic, we were able to do dense behavioral monitoring with video and audio sync to neural data and at home, we have participants control their own intracranial recordings through a tablet application and they reported their intensity of OCD symptoms using a slider bar on a phone application. One participant did a three-day long recording at home where there were natural exposures to OCD triggers on days 1&2 reflected by the log to symptom intensity on the y-axis. LFP availability over the 80 hours is shown by the orange shading on this plot. To analyze the LFP data, I computed spectral power over the two minutes segments of data around each rating. Here I'm showing results from that analysis. Spectral power versus symptom intensity across frequency means of interest for your left, CBS and CBS on rows 1&2. I found that the CBS spectral power shows correlations of those of the symptom intensity where the correlation between delta manpower showed a strong negative correlation with OCD symptoms. We've identified a candidate neural biomarker of self-reported OCD symptom intensity during natural symptom provocations at home. Where do we go from here? How can we continue closing in on biomarkers and validate this finding in a larger symbol? I think that our focus should be on how to collect behavioral data in natural environments that is just as rich as the neural data that we're already collecting. We need to identify temporally dense real-world behavioral metrics. All the work I just showed was done using self reports, really important but as Jeff mentioned, there are limitations of self-reports. Subjective experience can be different than observable behavior and again, it's temporarily sparse. If we want to know how brain activity is varying with changes in severity, we really need a continuous measure. I think this also reduces patient burden to report how they're feeling in every single moment accurately. These passive objective measures might help us elucidate the brain behavior relationships underlying why someone feels the way they do. To go back to our example on OCD, we've been working on identifying meaningful continuous metrics by using Alpha, as Dr. Berman described and so this is a still shot from the video that he showed. We saw a peak and positive affect, a smile of where DBS amplitude was increasing. This data and other data like this with continuous metrics, synchronized and neural data, I think could be harnessed to build machine learning models that predict behavior from neural activity or vice versa. The next action item on my list is that I think we need to incorporate multi-modal context of wear behavioral monitoring. What I mean by context wear is that some behaviors might be more quantifiable or observable than others depending on the context. Our goal though is to develop methods for quantifying behavior via multiple modalities that have high reliability with manual annotation. Here I've listed out some examples of behaviors that we could be monitoring and group them into different categories. If we want to quantify behavior during a social interaction, for example, only the social category would be meaningful to monitor. Whereas maybe during a workout, these more socially geared metrics might not be informative or even possible to encapture. There are some challenges with this though. One inherent challenge for developing these methods in searching for objective behavioral features during this science is that it's more exploratory and it might not fit into the framework of the traditional hypothesis driven study. I think this will require a really large n. It requires broad technical expertise, both in neuroscience and applying computer vision techniques and engineering. It raises questions about how to protect the privacy of the participants. I think it's also important to consider that there may not be convergence across different modalities. The third action item is that I think we need to explore the relationship between task-based in real-world behaviors and we need to be proposing naturalistic experiments that are grounded in findings from classic psycho-physiological tasks. Can we better align psycho-physiological task-based studies with ecologically valid observations to really understand the relationship between lab-based tests and naturalistic behaviors? Another example from my previous work in OCD is shown here. On the left, I'm showing a schematic for a task meant to provoke OCD symptoms through the presentation of provoking images. On the right, I'm showing a naturalistic analog of this provocation task where participant is working through a real life exposure of imagining a word on his hand during teletherapy session at home. Pairing task-based and more naturalistic experiments in this way, I think, allows us to ask the question are there mental processes elicited by the [inaudible 01:38:21] tasks that are relevant for real-world symptoms or functional deficits? I think this question is critical moving forward for identifying ecologically valid neural biomarkers of disease relevant behaviors. To wrap up all, talk a bit about the impact that this work I think might have on the field. I think that more dense behavioral information could enable precision psychiatry. Perhaps with better behavioral quantification, we can match individuals to treatments to understand why certain people respond to certain treatments. I think that more dense behavioral info could enable identification of neural biomarkers. Rich behavioral quantification would help us better understand the brain behavior relationships underlying psychiatric disorders and neural biomarkers I think it's serve as a more objective goal post for response to treatment. Lastly, I think that this more dense behavioral quantification could serve as part of the much needed bridge between controlled and naturalistic experiments. Task-based experiments allow us to observe and quantify behavior in a really controlled way and we need to approach behavioral quantification and natural environments with just as much, if not more vigor than task-based studies. Thank you for your attention.

Dr. Jeanine Simmons: For our last talk we have Lena Ting.

Lena Ting: Okay, great video, wait. Thank you so much for inviting me here. As a person who spent a lot of time realizing that the movements emerged from interactions of the bio-mechanics of body and the neural control systems, over the years, I've become clear to me that I have to move beyond thinking about movement as really just the output that we care about and to think more about behavior as it's been said before. This matches what was said before, but we really can't dissociate. It has been clear to me we can't dissociate cognitive function affect and movement because all of these things are intertwined as they're all helping us with our behaviors, which is solving problems in the world that have value to us, making decisions with incomplete information and taking actions in an environment that's dynamic. In my field, we talk about the nervous system generating internal models of the external environment that let us compute faster. These necessarily introduce biases in how we move that might show up as something we might refer to as our personality or our life history.The words associated with these show up in different fields in different ways but the basic idea is that when we look at behaviors and choices people make, whether they are cognitive or motor, the way in which we generate them are not necessarily, they're not objective. We're not going to be able to write down equations for them but they depend on interactions with the environment, on many timescales and the contexts in which those happen. Those are the things that came up to me when they asked me to please give a talk on how are we going to understand brain and behavior. I'm going to give you some examples and inspiration from where I drew inspiration from. To emphasize that we really want to handle all this data that's going to be different across contexts. We really have to understand the rules of the structures that we get and to understand the variability that we're going to get. Because it's not going to be as rigid and as my engineer brain would like. We'd like to in particular look at spatial-temporal data that are on the timescales of neural activity so that we can actually bridge multiple scales from neural activity to behavior. One example as you've seen that when we look at movements, I can measure joint angles and things like that. But in reality, there's much more information there about all social aspects and effective as we've heard. We can look at the data and break it down. We also need to start using biophysically based methods to look at, how does that even happen in the body? How do we get back down to mechanisms more? Here's just an example where the body doesn't change so we know that this is a physics-based model of movement with a control of it's changes and potentially a biologically plausible way so that person can express happy or sad walking across the various behaviors. We want to find the principles that it doesn't matter what movement I'm doing, there's something common that makes it happy or sad. To think about that better I want to go back to a pretty old example that I like to think about. My slides are not advancing. Which is thinking about accents when we talk. There's an objective space here of sounds, and this is one frequency and another, and each of these boxes represents the vowel sounds that we can hear when we're babies. As people interact with their environment, these spaces merge and fuse into new shapes that are irrelevant to the world. If there chunking them into different types of what we might call latent variable in today's parlance. But what it means is that there are biases that happen when people speak that I can predict an objective in quantifiable way. One example is that if you speak Japanese, then all of the sounds that fall in this region sound the same. When I'm listening to English, I can't distinguish these two sounds, and when I'm speaking them, I might say raw and law and confuse those two sounds. Those are things that we can actually measure happening in the brain, and the brain is warping this objective information. Then the context matters too so we can't think of these locations as being fixed in this objective space. But when a mother speaks to the child, the distances between these points stretches. We need to learn the rules by which these clusters, or units of action move around with individual, with contexts, and with mood. Getting back even further to something more linked to motor output. In my lab, we've looked at muscle activity, which is the output of the motor neurons, and demonstrated that in movement each person has a library of motor modules similar to these facial action units that we've just heard about. Then we construct movements based on coordinating a set of muscles across the limbs in order to perform certain biomechanical tasks. Now I was looking for something very objective here, and really had to concede that depending on the animal that I was looking at, or the person that I'm looking at, to perform the same tasks, which might be producing a force each animal coordinated their sets of muscles in slightly different ways. When we looked across people, these differ depending on if you're a ballet dancer, or if you've thought through rehabilitation, or if you have different neurological disorder. Perhaps that's one of the mechanisms by which we can identify different people just by the way they walk. But this far we don't have a direct linkage between these very static cartoons of different ways in which people activate their muscle activity, or different ways in which they might be impaired in movement. One way that many people have been trying to, is to now put these, patterns onto a biophysical model of walking. But we find that this biophysical approach is lacking, and that we don't know all of the neural constraints and neural dynamics. Even if we had a connectome, it would be very underspecified. We've recently worked with Gordon Berman to take this more data-driven approach to say I can see these differences in the movements, in these kinematic patterns, and when I compare them in my traditional biomechanical sense, everybody looks the same when they walk. There's more information that our brains are getting out that we're not capturing in the way that we treat biomechanics data. We can't go on through it, but we push it through a neural network. Then to capture the dynamics that is the spatial and temporal dependencies within data in a way that we can compare different individuals, and show that these people walk at the same speed or actually walk at different speeds that's the shading, maintain some characteristic of the movement that is theirs. Perhaps by now, looking at these two types of models of movement, we can hope to link this emergent behavior that we see with some more connected missed types of patterns that might indicate something at a lower level in the nervous system. I think this approach is going to be necessary when we are talking about how do we do multi-disciplinary research across species, and scale? To think about, oh, we'll have naturalistic behavioral studies to gather data and make hypotheses an experimental studies where we manipulate behavioral context. We have to be able to understand the structure of the variations that we're going to see it at all levels. Then ultimately again, if people have said to use technologies to actually perturb the causal mechanisms involved. I want to really just talk about really why this is so important. You recently got interviewed about the yips, which we may have seen at the Olympics, people, athletes who are unable to perform the motor task in a particular context, and it turns out that there are hypotheses about these being both bottom-up. Something about spinal networks going on all the way up to a prefrontal, cognitive reasons, as well as life history like early childhood trauma or genetics can contribute to these behaviors. This is what happens when you have to move in a real situation. It's just not about controlling your muscles. It also has relevance in clinical disorders. Freezing of gait and Parkinson's disease is similar in that people can walk most of the time, and different individuals have cognitive, motor, and emotional triggers that make them unable to actually walk and they freeze. When we think about how do we study that in an animal and make inferences, there's been some work by Steve Chase's group showing that they can set up an experimental situation where monkeys will choke depending on the stakes of the scenarios. Now that's only one way to look at it. When we think about these interactions, it's overwhelming. In my lab we've really just studied one behavior which is standing postural control, and started to measure brain activity, and based on some epidemiological work showing that cognitive state influences falls, we've been showing that the activity evoked during this very ecological perturbation to standing balance actually is really well-explained by some paper and pencil cognitive tests. It's probably modulated by effect. This is something we have to recognize because often when we see patients, they're not feeling well, the dirty secret is, we don't measure them or we don't save their data when they're like I'm having a bad day. Because we don't know how to take that into account. When we are comparing the data. We'll also have to recognize bottom-up mechanisms, which is that, we're looking at even the sensory information that's coming up from the periphery is modulated by motor cognitive state and training. I just wanted to say that neurodiversity and variability is really important to understand and not try to find some unique mappings between brain and behavior. That by understanding the structure, we can hope to find principles that can go across lots of behaviors, scales, and species. I'm just encouraging people to collaborate just like this workshop, and thank you.

Dr. Jeanine Simmons: Thank you. We are now moving from the individual talks to the discussions of this model. Well, go-ahead

Speaker 17: I was just going to thank all those amazing speakers. It's been a really interesting set of four speakers. Well, actually five speakers. That was an amazing initial kickoff introduction. I want us to note a few themes that were throughout the four speakers. The first or two of the speakers focused on movement and provided incredible multi-modal, deep behaviorally dense quantitative metrics on movement, both from the human perspective that Dr. Ting just shared, as well as a couple of different animal, other animal model species, zebrafish, rats, insects or Drosophila that Dr. Couzin shared. Then we had two speakers where we were discussing or they were sharing data on internal states, and trying to find bio-behavioral markers to predict internal states. It seemed that while we had great information on internal states, we had relatively few realistic bio-behavioral markers to predict that well. Dr. Cohn's example was fantastic, where he went from only being able to predict 8-17 percent of variation in OCD, up to 60 percent when started to take in greater repertoire of multi-modal inputs into that. There will be multiple panelists bringing up different questions, but I wanted to really emphasize the ending theme from Dr. Ting's talk about, how do we identify rules and principles? How we have to go across multi-scales and different species to do that. As a neuroethologist, I want to throw out the question to us all, are we at a point where we need to abandon studying the specialist? Or from a neuroethologist point of view that would be invoking Croak's principle, a Danish physicist from over a century ago who put forth that for every problem we have, there's one particular species or taxon that we should best study to find the answer. Do we want to change tactic and look more generalist or perhaps, and I would be in favor of this, going extremely comparative? Neuroethologists, we often pat ourselves on the back if we compare two species. But it seems, just as Dr. Ting just showed us, there's multiple ways to solve a movement pattern. Can we look across multiple species of brains, different species with different brains that solve the same problem in different ways, to actually enrich our ability to solve problems at the human front? I just wanted to throw that out there to start. If anyone feels like chiming in on that, I think the idea is you unmute yourself. This is not meant for me to talk for eight minutes.

Speaker 18: Should we put our videos on?

Speaker 19: Yes, please.

Speaker 17: Or should we stick with specializing? Are there things that the rat can tell us more and we should just dig deeper into the rat or the Drosophila to find insight into humans?

Dr. Jeanine Simmons: Let me just start by saying that these affect the decision-making, movement, and effect, are not special to humans. Something has to matter to you to be able to want to make a decision. So in that sense we're going to find it in many different species, but to different extents.

Speaker 20: Well, it's interesting that the two talks that use DBS, they're stimulating parts of the brain that every vertebrate has. There are ways to figure this out with DBS at level across lineage comparison. On that theme, again, drawing from Dr. Ting's work where she found that different animals, different humans, use different coordinated modules to produce the same walking speed. I think by becoming more comparative and looking across brains that have solved whatever problem we are facing, changing one internal state to another internal state, we can actually identify different brain regions and pathways to do that. Now whether or not the solution ends up being DBS or the solution ends up being pharmaceuticals, that can stimulate different neuromodulatory pathways to affect outcome. Is another way to look at that.

Speaker 21: I want to be clear though that it's what we see is shaped over long periods of time, and learning, and rehabilitation. I think this happens in DBS for depression too. There's an instantaneous change that might happen with neuromodulation that enables a longer-term slower time constant of change in the units that shaped somebody's behavior.

Dr. Jeanine Simmons: Great. Karen Rommel, I can't see part of your name.

Dr. Karen Rommelfanger: Karen Rommelfanger.

Dr. Jeanine Simmons: There's the rest.

Dr. Karen Rommelfanger: Thanks. I really enjoyed this opening panel and I have a lot of curiosity, particularly around Jeff Cohen's work, where he noted that the AFR or AFR, not sure how you'd said it, was optimized across cultures, and then also close with an opportunity for us to explore that more contexts were needed for exploring how this technology would work. Certainly more data would be needed to optimize the technology, capabilities, and applications. I'm wondering if you could share a bit about the biases that have been acknowledged in the work as it relates to socially constructed identities through like race, for example, and gender, and the degree of confidence in the interpretations across behaviors. We focused on mood here, but also opportunities for looking at pain and other subjective states. Wrapping that together, what are the opportunities and challenges for a technology like AFR in the brain behavior synchronization model in light of those questions around bias, opportunities, and limitations?

Dr. Jeffrey Cohn: Thanks for the question. [inaudible 02:00:21] in detecting action units. Action units are descriptive movements, and the way that walking is a movement. It's primarily descriptive rather than it's inferential construct. We talked about gender or cultural identity or affect. Those are highly inferential. We need some bridging in order to support inferences about the meaning of action units. Now just with respect to descriptive meaning, we do actual unit detection in infants. Infants have very different shaped faces, they have different movements, and yet the system works because it's primarily anatomic and it's been trained on infants. For people with very dark skin, AFR [inaudible 02:01:25] so far, it appears to work well [inaudible 02:01:31] because it depends on the amount of lighting. But it's really [inaudible 02:01:38] When you have stimulation in the ventral striatum, I think that supports an inference that you're eliciting positive affect. I make that inference, but I'm making it from what I know about particular combination of action units that have been studied broadly in an effect of context.

Dr. Jeanine Simmons: Thanks, Jeff. I think we need to move on to the next discussion. But I think there were several questions around, and I think we can generalize about when we're studying behavior, in which situations, at least in a few minutes, do we need to think more carefully about how we do that based on race, ethnicity or [inaudible 02:02:24] But now we're going to move on to Timothy Wright.

Timothy Wright: Thank you. I want to thank Molly for starting us off. Damon, thank you for putting that up. I wonder if we could just take it off, it might be more useful to see the whole panel right now, and then towards the end of my time, I'll ask questions specifically about that. Thank you very much. I want to continue on this theme of affect and the difficulties we might have with systems that are developed for one species or one subset of a species. Think about how we can expand that approach into a comparative fashion, so thinking about other species. It's clear people working with humans have thought quite a bit about the importance of affect, and animal behaviors are not blind to this. There's some well-known affects like if a cricket has lost the fight earlier, it's more likely to lose a fight later even if it's a relatively easier opponent. But clearly trying to figure out what affective state is in animals is a challenge. I want to start with the human-oriented panelists, we're all human I guess, and ask what potential they see for using these approaches with animals. Then I want to move on to Ian and Molly and Vince, all of whom have worked with animal models. I'll throw that out to Nicole and Jeff and Lena to start with. I see Lena has got her hand raised.

Lena Ting: I'm not sure about affects, is just that I'm sure that's true, there have been some interesting studies in guinea fowl by [inaudible 02:04:10] showing that the personality of a guinea fowl affects how they walk around the room or how they slide, or how they care about crashing into things. Like I was saying, I think you're going to see that in many animals. The cats that I trained all had different personalities which I very much think affected their muscle coordination patterns that they used and how they use them.

Timothy Wright: Okay. Any other comments from Nicole or Jeff? Go ahead.

Nicole Provenza: I think that one, I guess interesting concept, well, it's shifting my mind from thinking about humans and thinking about animals. Obviously you can't ask animals how they're feeling, however you can ask humans how they're feeling. We have to infer everything we assume, I guess, about how animals are feeling based on their behavior. I think the idea of doing that in humans is really cool. But one question I've been chewing on for quite a while and I'm sure a lot of people have thoughts about this is; what comes first when someone is recovering or getting better if they have depression, is it their behavior changes and then they feel better? Does it happen at the same time or do they feel better and then their behavior changes?

Dr. Jeffrey Cohn: I would say we get the special status to feeling to the subjective experience, that is the sine qua non of emotion. But it's really just one aspect and it's very hard to know what your pet is feeling, it's very hard to know often what your cat specific is feeling. But there are other aspects such as reaction tendencies. You saw the cricket that loses a fight and then goes on to lose an easy fight, that seems to me like an affect of response. It's an emotional response that the experience of losing that initial fight affects its ability to coordinate aggressive affective behavior in conflict. That's emotion. I don't know what the cricket is feeling, but I would say that certainly it's not high on approach, it's not exhibiting mastery of which it's capable. These are affective responses.

Timothy Wright: Vince, did I see a hand raised earlier from you?

Vince: Yeah. I've seen such contexts but I could translate it if it's of interest, but otherwise I'll let other people speak.

Melissa: I'll just chime in from the non-human animal characterization of behavior.

Vince: But that was the angle I was going to take too Melissa.

Melissa: Okay. Well, I was going to say your work as well pitch similar. How we actually capture internal states and affective internal state of a non-model organism at this point, is doing genomic profiling of the brain. Ian gave a great example where you can pair behavior with transcriptomic profiles and understand what's going on dynamically at the brain, not at neural stimulation but gene pathways that are being evoked in the last 30 minutes of the animal's life or less than that. We actually can identify gene suites that do diverge, we don't know in terms of affectation exactly what they represent, but we can pair that with movements which we can surmise to have something to do with either fear or excitement or other continuums of behavior. That's how we do it. Instead of self-reporting, we look at what's going on in the brain, not at the level of neurons, but genomic profiling often.

Vince: Now I think that this problem of bridging from human studies to animal studies is really key and central, at least for much of what I do. Ian said he was studying autism in fish and we're studying it in the rats. The question is; how do you validate these approaches? How do you know what you see in a human patient is anywhere near what you see in your animal? I don't know what mechanisms we have for facilitating comparisons between the human condition and various animal behaviors. But perhaps one approach is to study rather low level manifestation of high level phenomena which can indeed be compared across species. I'm thinking here of movements and the autonomic nervous system function, because that gives us at least something to compare in a more of an apples to apples manner. Perhaps also use similar techniques for measuring and similar analytical frameworks, so that the comparisons can be made more easily.

Dr. Jeanine Simmons: Vince, I don't know if that was the beginning of your actual formal discussion comment. But because it is time for you, I just transitioned organically.

Vince: I think this is a big question that I've struggled with. Listening to the speakers, I realized that there is a gulf in approach and mindset and techniques and frameworks between those who study human disease and the clinical manifestations and those of us who do mechanistic studies in animals, that we try to simplify things as much as we can and then make inferences about what we see to complex human disorders. I don't have a particularly good remedy for that, but I would love to hear from those of you who study human disease or disorder. If you have any guidelines or criteria for validity of the various model organisms that we study. Is it as Molly said, is there a particular animal model that's particularly well-suited to study OCD or depression? If so, what are those criteria? How we should think about this.

Dr. Jeanine Simmons: [inaudible 02:11:48] .

Iain Couzin: I guess I put my hand down and then up again, might be misleading. I think you make a really good point. From my reading, most of the pre-clinical work, that's been done on psychiatric illnesses, they've done a very good [inaudible 02:12:07] But I think with respect to an organism like zebra fish, you have a much higher degree of control. We can put them in virtual reality. Second, infer causally works algorithms on this function, that's the critical things about virtual reality. You actually determine precisely which algorithms that work. Then by collaborating with people like [inaudible 02:12:29] to your university, we can then potentially look at circuits that might be affected, but I will say this is like a fishing expedition or it's not the fibrocytes I like to do because we have magnitude knockouts. But the more we look into it, it's like screening just to see if we get lucky. But the more we look into it, the more I realize that we might get lucky. Sorry, can you hear me now?

Vince: Now, I can hear you Iain.

Iain Couzin: Sorry about that. There are these basal social behaviors at least that we could study, and I think the answer to your question is we don't know if it's going to be useful. We don't know if it's going to be clinically useful. But zebrafish are highly complex in their social behaviors, people have completely misunderstood how sophisticated they are because they looked at them in an environment that doesn't allow them to be sophisticated. I think they might be a good model, and I would say, one of the things I was thinking in my talk, drosophila and [inaudible 02:13:44] . You probably never really be able to understand them in the field. Rats and Zebrafish we can do that with fish, we can do that with rats. Yet no one is working or almost no one is working on zebrafish in the field, why not. Maybe we need to push this connection between these skills. I don't see a problem with using a very strong model organism like a rat or zebrafish to make these powerful connections across scale. Because we can't just randomly just, I think the other thing that was mentioned is choosing an animal for a specialist capabilities. I think Molly mentioned that. Absolutely right, fully agree. Completely agree. That's really important, we need to have non-model organisms absolutely. But with the model organisms that we do have, can we maybe consider programs that span from the wild to the lab because I think the types of technology, that I've been hearing about today, could be applied in the near future, if not now to naturalistic conditions or even natural conditions. I think understanding how rats behave in the world could be a phenomenon. That's why if my feelings, at least to say. I think we can combine these works in a very synergistic way.

Molly Cummings: I was just going to pause it that maybe we should get away from specialists and actually try to study many more species, find the lowest common denominator if we stay with depression, some simple behavioral marker for withdrawal, and then identify the same components that are operating, or different components that are operating across brains in different lineages. I think that might be a simple way to find a treatment. Iain, your system is amazing, but not everyone can create the holographic and test it to the level of resolution that you're providing. I'm wondering if we could go almost the other direction.

Iain Couzin: If I could just quickly before Paul speaks, just mention that I took this slide out because of time, but I think democratizing these technologies and making them cheap and easy for everybody to use is a huge priority for us. So I'd be surprised if in five years time we can't produce a system that anyone can use with this technology, but Molly I also fully agree with what you said. I think having an evolutionary perspective, but they're not mutually exclusive. That's the thing if one could look into certain systems and cross the scales and also look into the diversity of the wonderful biodiversity we have to really understand things.

Dr. Jeanine Simmons: Paul [inaudible 02:16:21] .

Paul: Hi, Yes, I would also like to echo what Molly just said. I think looking at a wider range of species is very important. In particular, I think we could be a bit more strategic in picking the species. In particular, I think without denying the value of convergent evolution, we don't want to study social behavior, for example, in bees, may give us a lot of interesting insights, but it's definitely evolved independently from social behavior in humans. Also probably for, in the case of other animals, dogs, wolves, etc. I think we should pick species on the basis of the window they give us into shared mechanisms that concern us. So in that sense, species that diverged from us at a particular moment in the past, but then did not change too dramatically. In that sense, actually, zebrafish they're wonderful. But they really did change a lot. They duplicated their genome. They changed their fore-brain dramatically develop mentally. They came up with a lot of things that their or shared common ancestors did not have. Birds likewise, they developed all kinds of amazing things but totally independently. I think we'd get more out of studying some species that are highly neglected. I think basal vertebrates like sharks, that did not change so much. If we pick the right species, lizards, and other reptiles. I think blocking on this name. But it said recently in neuroscience we use to study many more species, and now we're becoming monkeys, rats, zebrafish, and drosophila. I think we need to look very broadly, and I think we can pick specific species based on their phylogenetic relationships while still being broad. Again, I would like to also acknowledge that of course, part of the reason we specialize is simply because the more people study a certain species, the more easy it is. I studied rhesus monkeys because so many other people do, and I can draw upon all that knowledge. But it would be actually useful to do something more like, for example, what Leah Krubitzer does or John [inaudible 02:19:11] does and study many species of primates. I think that would actually give us insights into the things that are relevant to humans.

Dr. Jeanine Simmons: Thank you. I think we're going to have to wrap up. I'll just want to say a couple of things. One sounds like there may be some more room for discussion about which species we want to be studying and why. But there's definitely some agreement that studying multiple species, and considering prostheses studies is important, and I would argue within the context of this workshop, it's important to think about how do we measure different behaviors with different species. If we want to study sharks, how are we going to measure sharp behavior, if you want to study zebrafish how are we going to measure zebrafish behavior and how are we going to measure human behavior and so on. We are keeping the question instead of fitting the chat and Q&A for to seed tomorrow's breakup sessions since we haven't had time to get to all of them now. There's so much given a chance to talk about, but for right now, we're going to move on to Panel 2, which I think [inaudible 02:20:15] .

Speaker 5: Thank you Jeanine. That was a wonderfully rich discussion. Difficult act to follow, but it is my pleasure to introduce Panel 2, which is on sensing behavior in its environment dimensions in dynamics and is shown on the slide. The central question for this panel is how do we capture the information needed from individual organisms so for groups, in physical environments, so that we capture the complexity of behavior. So really the question and one way to translate the big question is, what are the different types of data are needed to build models of behavior that reflects the multidimensional complexity of behavior in the context in which the behavior occurs naturally? An idea that came up extensively in the previous panel, and what are some of the technologies in particular sensor technologies, what are the informatic tools that are available, and which ones are needed in order to collect and integrate these types of data to build a useful conceptual frameworks and [inaudible 02:21:26] models. With that, the speakers that we have about lined up here. [inaudible 02:21:31] , Galit Pelled from Michigan State University, Ben Hayden from the University of Minnesota. Malcolm MacIver from Northwestern University and Raji Baskaran from Manifolds Lab. Then we switch over to the discussions, then [inaudible 02:21:48] discussion for Panel 2 are Peter Hartwell from [inaudible 02:21:51] InvenSense. [inaudible 02:21:52] from Harvard Medical School and Andre Green from the areas of Michigan, [inaudible 02:21:59] . With that, I handed over to Galit.

Dr. Galit Pelled: Hi, I'm Galit Pelled in Michigan State University. In my lab, we're interested in neural performance, which is the practice of improving motor function that will lead to higher levels of speed and strength and cognitive functions including decision-making and learning. To get there, the movement and the cognitive processes are defined as behavior. To understand normal behavior and to assess changes in behavior, we need tools to measure behavior. There was a great discussion before, whether we should be looking at diverse animal models to understand behavior. In my lab, I will show you that we argue that this is necessary. Here you see in the next few slides, I'm going to show you tools that we're developing and concepts that we are studying in more controlled neural systems and how these may be adopted to more complex systems. Understanding decision-making and goal-oriented movement is really a major goal of neuroscientists and behavioral scientists. These are of course, integration of very complex the brain and the peripheral nervous system. Here you see an octopus in my lab, there are 300 species of octopus. This is the octopus bimaculatus, it is actually the only species of octopus that its entire genome has been sequenced so you can imagine all sorts of amazing things that we will be able to do with that in the future. You can see it here in its thing, interacting, trying to grasp the finger of one of my students, and it's quite amazing. We're trying to study octopus grasping movement and we're hoping to identify the algorithms that describe how the octopus initiate and execute the movement. How is it that octopus can adapt its movement midway and can we develop new type of bio robotic devices that will be rapid and adoptive, such as an octopus arm. The octopus is an amazing species in so many ways; it has the heart, it has blue blood, it camouflages, it regenerates and they actually existed. There's the first fossils of octopus dated 296 million years ago, so even before dinosaurs. In the course of evolution, the octopus quite amazingly came up with many similar solutions for physiology and sensing like vertebrates. For example, its eyes and it's optic lobes are very similar to the vertebrate systems. But in terms of motion and movement, it developed a completely alternative strategy. It has a huge nervous system with 500 million neurons so similar to what a dog has. But most of the neurons are not in the brain, they're actually in the arm and each single arm has an axial code that act similarly like a spinal cord. Most of the decisions that the octopus make is not in its brain, it is making it in the arms. A disembodied arm is known to keep moving in a way that an intact octopus does. You can imagine how the octopus now gives us really an unparallel way to look at neural patterns in neural networks that are associated with movement. Here you can see that we're using AI with DeepLabCut, we can place already 16 makers on a single arm to measure movements. There's eight arms, there's constant movement, there's constant allegation and shrinking. Really if we want to measure the octopus movement at its natural environment, DeepLabCut is a good way to start with, but to get very high resolution kinematics, we have to go and use different techniques. What you can see here that we can use reflective sensors, reflective markers on an octopus arm. On the top it's an arm outside of the water and now we can also use in an octopus inside the water. I'm not sure we can see the movie. Thank you. Reflective sensors outside and of course inside the water. But as neuroscientists, we also want to have the neural correlates that we record at the same time with the movement. For that today we can place array of electrodes inside the octopus arm. You can already see here we can report more than 16 channels at a time for an octopus arm and we can start seeing different patterns in terms of the amplitude, in terms of the frequency when we give different types of stimulation. Central stimulation, profile stimulation and so on. But of course we want to record all of that in an intact octopus, in its natural environment when we can provide natural cues and stimulation. Now with [inaudible 02:28:08] we worked on developing a miniature wireless multi array recording device that we will be able to implant in an octopus arm and have the octopus and its big tank recording action potentials and at the same time recording its motion. We can even go deeper and look at the neural network in single action potentials. Can we please play that video the top-left? We can place a slice of an octopus arm on a multi-electrode array. This dish has 26,000 single electrodes, and you can see here that we can deliver either a central stimulation or peripheral stimulation and we can start seeing different patterns of activity. All of that together hopefully will enable us to identify the circuits that are associated with grasping how is the octopus having adaptive grasping and changing its motion midway, and will we be able to identify these algorithms and test them in flexible material based by [inaudible 02:29:46] I showed you how we can use these high dimensional technologies.

Speaker 5: One minute.

Dr. Galit Pelled: Yes.

Speaker 5: One minute left.

Dr. Galit Pelled: When we measure in the octopus that has special challenges because it's inside the water. In my lab we're also interested in other animal models and how we can assess behavior in large animals. We're specifically interested in brain injuries. Over the past few years, we developed Yucatan mini-pig model of brain injury. I just want to show you very quickly how we're using exactly the same methods that we're using in this unconventional species to more perhaps conventional way. You can see here again, we're using the DeepLabCut to look at motion, to look at locomotion and the location of the pig inside it's arena. We using the same type of motion reflective sensors, and you can see here the pig with marshmallows it's going to behave very well. Also we can get very high resolution kinematic data and data analysis of pig motion before the injury and after the injury. Our pigs also wear wearable sensors. They are wearing Fitbits so we can tell how many steps they do a day, when do they make these steps, they're are, of course, in their natural environment. We can also measure how much they sleep a day, when do they sleep. We have video cameras to look who they like to sleep with, and so on. I didn't include that, but we're also interested in personality changes in pigs and they have really very developed personality. We can measure aggression and depression, and anxiety and short-term memory and long-term memory. We really develop a whole array of technologies that we can measure in these species. Just to conclude, I showed you that we developed tool to record behavior perhaps in unconventional species and in less conventional environments, but hopefully this will be able to be adopted in more traditional species. The concepts that we're going to learn will hopefully translate to really understanding of human behavior. Thank you.

Speaker 5: Thanks very much, Galit. Ben, ready to go? Quite.

Ben Hayden: Thank you very much. Thank you for inviting me to come here. Title of my talk is the behavioral imaging revolution. Behavioral imaging is just a term that we use in the lab just to refer to what a lot of the things people are talking about today is about, basically the use of cameras and downstream software and technology to say something really sophisticated about behavior. I just want to start with one thought. Which is that, before the telescope was invented, you could still see the stars just fine. The difference between the telescope and your eyes isn't that they let you see something completely new, is that they let you do something a whole lot better and see a whole lot better orders the magnitude better, and that's really what led to the revolution 500 years ago or whatever that is. I think the same thing is happening right now in behavior. Let's see if I can get this video to play here. This is just a video of a monkey at the field site in Cayo Santiago where I've done some fieldwork, and what really strikes me and always has struck me about monkeys in the wild is that they're just generating enormous amounts of data. This data is just leaking out of them constantly, and I'm like how do we gather all this data? I've been trying to figure out ways for a long time to try to do that. Everybody has been saying it already I don't need to repeat it, but the data they generate is not just interesting to primatologists, but also biomedical researchers, psychologists, neuroscientists, and apologists, a bunch of other things too. Of course, that's really what this symposium today and tomorrow are about. In my lab at the University of Minnesota, we have our own bespoke system for studying monkeys. This is a picture of a monkey in our cage system moving around, interacting with some [inaudible 02:34:38]. We have 62 cameras tracking him. We have a bunch of software that we wrote to do that. My goal today in my brief time is just to talk about, how do the consequence of tracking the monkeys and the ability that has to do behavioral imaging just to see what the behavior is. The way that it's changed our thinking about how to be neuroscientists. Of course, we are fundamentally interested in the relationship between brain and behavior in my lab. I know this is a broad meeting with a bunch of people, so not everybody's thinking in terms of that. I just want to emphasize that, basically, we want to see how brain activity predicts and drives behavior, and of course, that's not easy even with high-quality behavioral imaging, you have to worry, for example, about confounders. You have to worry about things that are correlated with the thing you're interested in, and that may also be driving the neural activity. You do things, do standard things like careful task design, big data, even bigger data, more sophisticated analyses. We do all these types of things in order to deal with the problem of confounders. But the real thing that just keeps hitting us in the head as we do this research in my lab is that the ability to measure behaviors is just like the ability to look at the stars with a telescope, leads to different questions. It almost forces you to ask different questions. They find different things to be interesting than you would otherwise. In the case of a monkey, typically the way we've done experiments for like 50 or 60 years is have them sit in the chair and just do a little task with their eyes. With our system in the big cage, the very first thing we did, we took huge amounts of data, hundreds of hours of monkeys moving around performing a foraging task. We did some preprocessing. I'm not going to go into that. Then we did a simple dimensionality reduction and clustering analysis on the behavior, and we find that the behavior of the monkey moving around naturally divides into these 49 [inaudible 02:36:39] . Numbers are not particularly important, it depends on the way you do the pre-processing and stuff. But you get these discrete [inaudible 02:36:46] of behavior that correspond really to natural things that you see in the behavior. Then these, of course, have a hierarchical organization. This probably shouldn't be too surprising. What might be a little more surprising is that we have the monkey do a task or a different task or tasks off, and we see the subtle changes in the structure of this hierarchy. I'm not really going to talk about what that means today except to say that the key point of this for this talk is this isn't even a question we would've thought about asking if we didn't have behavioral imaging if we didn't have the ability to do high-quality, high-resolution tracking and behavior when your monkey is sitting in a chair doing a task you just assume that he's in a state of doing the task, and the behavior is just either on-task or off-task. But you can see there's actually a very sophisticated complex structure of behavior, and now we're starting to look at the neural correlates and that kind of thing. I'm going to give you one more example just to illustrate the way that behavioral imaging helps you think about and ask new questions. The core topic of my lab's research is about economic decision-making. Basically how human or a monkey in our case, will choose between things. The way we do this is based on microeconomic theory typically. You are sitting around doing nothing and then all of a sudden two options appear and then you choose between them and then it's over and your choice is over and that approach to thinking about what a choice is leads to these very discrete categorical models of how choice works, and the implication of that is that these are going to each correspond to some brain area and that drives the shape of the neuroscience of economic choice. Again, to emphasize the theme that natural behavior driven by behavioral imaging leads to completely different conceptualizations of how these things work. I tend to think of choice in a very different way. I think of it as continuous. I found this video of a couple of dogs chasing a rabbit. This is what I think of as the economic decision-making in the real world. The dog is having to choose exactly which way to go at every single moment, and it's a continuum of choice and the continuum of possible actions. He has to decide higher-level things like what strategy he's going to employ to follow the rabbit. These are things that you could in a really clumsy way do with microeconomics as a foundation. But it really wouldn't be a very natural fit. This has lead our lab towards thinking of engineering control theory as a foundation for thinking about what's driving behavior. It's been very pleasing for me to see the talk so far today have also, a lot of them have converged on the same idea that really we need to use control theory and feedback as a way of understanding how decisions occur. I'm also going to talk about one other thing. Just to get one more example in the natural world. In the laboratory, if monkey or your person is sitting there and you explain the whole task to them. They understand that they've been doing it for months and months after a monkey. There's no doubt or uncertainty about the structure of the task in their mind. But in the real world, we're constantly basically starving for information. We're highly under-specified, and I put this picture of a monkey trying to drive a car because this is how I feel in my life. I'm basically trying to do really complicated things that I'm woefully inadequately prepared for, and I'm constantly needing information, constantly seeking information so much so to really drive pretty much all my decision-making. I think this is actually something very fundamental, and it helps explain just, for example, the way that monkeys deal with uncertainty isn't particularly well-described by microeconomic theories. We've had a lot of trouble with that we've been doing that for 15 years. But incorporating concepts of the need to resolve uncertainty has actually helped us understand that kind of behavior a lot more. These are just a few examples of the way that taking this naturalistic perspective, which is really ultimately an evolutionarily driven perspective, it helps us to think about things in a different way, ask qualitatively different questions. Then inevitably those are going to give us different answers. I'll just say one other thing. I have a one-minute warning. I'll just say very quickly that we in a lot of other labs have started recording brain activity in these more naturalistic, freely moving tasks. There's ton of phrenological model of the brain where we have about 150 areas that each have some particular function. It doesn't really work as well. Actually, a lot of these brain areas seem to just have a Frank motor function when we have the monkeys moving around in the real world, that seems to also be true for rats and mice as well. That is causing us to try to think of ways to rethink exactly what brain structures do and how they relate to each other. But again, we wouldn't have done that. We wouldn't have been forced to do that if we didn't have all this data coming in from freely moving monkeys, driven by the ability to image their behavior. Let's see, let us say in the future we're going to be doing experiments more and more towards this world about a monkey. Brain embodied within the body of the monkey and embedded within a complex natural environment, and that is really going to help us do neuroscience in the 21st century. Thank you.

Speaker 5: Thanks very much, Ben. Malcolm, are you ready?

Malcolm MacIver: Yeah, here, can you hear me?

Speaker 5: Yeah.

Malcolm MacIver: Great. Let me share my screen. Do you see my first slide?

Speaker 5: Yes.

Malcolm MacIver: Great. So my name is Malcolm MacIver. I'm very happy to have a chance to talk to you today. Topic of my quick talk here is widening the aperture of behavioral research. By this I mean, 20 years ago when I finished my PhD in decision making neuroscience and other areas of behavioral research, we settled on fairly idealized approaches to alternative force choice, this kind of thing to make the task somewhat easier to manage and control and similarly at the neural level, recording single neurons at a time or modeling them with compartmental models was pretty common. What's really cool in the past 20 years has seen the aperture widen to encompass some of these things. Naturalistic behavior is coming on strong. Whole animals stimulation, I'm going to advocate for today and we see some of them in the field. Evolutionary approaches we've heard a lot about today. Some robotics, and of course there's lots of other things, genetics approaches I don't have on here. I didn't want to get it too messy. The question is how to operationalize the consensus that has emerged into actionable intelligence for those labs wishing to pursue it if they're not already on this track. To motivate my approach, I think it's useful to point out that the body is a co-operative ecosystem of about

40 trillion human cells and another 40 trillion bacteria, viruses, and fungi. So about 0.1 percent of these units are neurons. Behavior is the output of this entire ecosystem. So a study is a really cool opportunity for putting our arms around the entirety of the organism. To make this point, I love this video of a passive dynamic walker from 20 years ago as well. This is a robot that has pretty much the same dynamics as a human walker yet there's no motors here, there's no control. The only input of energy is this inclined plane and it gives a form of a default dynamics almost for free. I think what this point amounts to is essentially that the body throws everything it can at the problem of survival, of course, and we have tissues that have very low energetic footprints, 0.2 watts per kilogram like boom that handled regularities on the order of billions of years of gravity, dealing with movement on the gravitational field. Then neurons really specialize on contingencies at the millisecond time span, and of course very important, but we need to open our purview to the whole thing. Computations like spread over the entirety of the domain. So how do you do this? How do you broaden it? I'm going to argue, well, using tools of synthesis, this is not really novel, but how do we actually use them and what are they? Point is, is that counter-intuitively, what seems to be making our job harder by incorporating a whole other bunch of aspects of an animal actually does make it easier in the end. Some of these engines of synthesis are organism and environment simulation, robotics, and evolutionary approaches and virtual reality. I'll give a couple of case studies of that. Here's some really old electric fish work that I did from my PhD, and the idea was to reconstruct signal input, which is fluctuations of transdermal voltage as the animal is doing a naturalistic task, which you use motion capture data and then you synthesize within a computer models of electric image formation, where the sensors are on the body, an electric field model, a model of the prey that the animal hunts in its natural environment, and then a behavior model constrained by empirical data collected from the preceding step. Then you get voltage histories from a spike model. You can get spike trains and ultimately we get through a lot of computation. The afferent spike trains across 14,000 afferents of the animal. We can do that not only with active electric sensory. I'm getting a lot of weird sounds from another speaker I think maybe. There we go. Not only are we getting input across 14,000 electric sensory afferents, but we can basically follow the same process to get the passive electro sense afferents and then the mechanosensory afferents as well and look at how they're activated during natural behaviors. Then we augment this with a robotics approach to look at how movement is being constrained by the animals, by mechanics, how the animal has to re-generate the thrust that it's generating and we use those data to constrain numerical models to do even finer resolution analysis and we do the same thing in the sensory domain with some sensory robotics. I don't really have time to go into, but it can navigate autonomously through these plastic pylons using electric fields. Now, the payoffs here, well, behaviors that made no sense at all when looked from a strictly sensory processing perspective or information theory perspective, once we augmented the ways that the animal generated thrust and how much cost that cost energetically, we could make sense of behaviors that did not make sense from the sensory or information theory perspective. So obviously the animals can jointly optimize in all of these different factors but we had zero insight into what they were without that more synthetic approach. The second payoff I mentioned is that there was a big change as a result of characterizing the signals through the synthesis approach. A big change in the way that signals are fed into the nervous system of the electric fish in neurophysiology labs. That in turn has led

to discovering neural processing strategies for prey related signals versus communication signals. So I'm quickly going to talk about some evolutionary work where we discovered that during the transition on the land, animals tripled their eye size and so there's an idea that perhaps aerial vision led to terrestrially. That got us thinking about how the sensory ecology of animals in water versus on land leads to different decision-making strategies. In particular in water, we have these sensory bubbles that are very tightly chained to the animal and very short and they detect a predator and have to fire off their [inaudible 02:49:39] within a few milliseconds to survive. With the long sight lines that land provides, you can imagine an animal who now has a much larger sensorium being able to evaluate several different trajectories and pick one to get to safety, in other words, planning. We're doing a lot of simulation work on that. I don't really have time to go into. But one of the things we've found is that in medium entropy or medium clutter environments that match the savanna environments that humans went into after they split off from chimpanzees, we find that planning reaches its maximum advantage over environments of different cluttered geometries. So right now we're busy testing this empirically using a robot that has a CO_2 cartridge for air puff dispersal and mice and so here you can see that air puff working there when it turns red, getting the mouse to run away from that and hopefully re-plan a route. So we're doing a lot of analyses right now of points of slowdown in the habitat as to whether they are actually engaged in planning behaviors. So you can see a few indications of that. There's a phenomenon called VTE in rodents where they do basically a head wag and you can see that happening here at this choice point as it senses a robot nearby. So let's see. Now, since a lot of people are interested in human work here, I wanted to mention we've translated this paradigm into a human virtual reality system. This is the view when you walk in and the predator now is a scary looking ghost. We have a wireless system for VR and every movement, every foot that you take, every foot that you move in real space is matched in VR. So here's a person in our virtual reality environment matching the one that the rodents are going through and they're running away from the predator as well, using the same approach of moving around the obstacles to be hidden. So now we're able to prepare trajectories taken by humans. Just a few samples right now we've just started this work, two mice and start to do comparative work on how these two animals do planning in complex environments. I just want to end on a note that I think that it's very interesting to me that collaborations in particle physics go to 5,000 coauthors and particle physicists that I know who knows something about neuroscience, thinks that we're working on a much harder problem. I wonder whether we need a couple of ordered of magnitude more cooperation in terms of our effort to make faster progress and I think this is where this workshop can really help out a lot, and a few points on how you might add engines of synthesis when they're not native to your tool kit. I have a few points on that. Essentially, doing a sabbatical, attending a conference to see what's likely to intersect with your collaborator, and finding a person newer in their career. These are all but approaches that I've found very helpful. As I've done a huge number of collaborations for the work that you've seen. I'd be happy to take questions later during the discussion section. Thank you very much.

Speaker 5: Thanks very much Malcolm. Our last speaker for this session is Raji, are you ready? Take over. Thank you.

Raji Baskaran: Thank you. Good afternoon, everyone and thanks for this opportunity. Now I'm going to completely switch track. It would be understatement to say overstimulated in the last couple of hours but I'm going to try to keep lingo of both the engineering domain where I come from, and the business and real-life application as little as possible and keep it very plain. Today I want to talk about two main ideas, both themed around multi-scale sensor fusion. As I see, I'm a micro-scale sensor technologist, so miniaturizing things and making it possible to collect the larger and larger data sets that you all really love. [inaudible 02:54:00] is kind of where I grew up in. But I do want to say Malcolm. One thing I recognized [inaudible 02:54:06] robot I do my masters in Cornell, around the same time I was there and I know that robot personally in a lab next door, and I'm a dynamics person, so I really enjoyed that aspect of it. Today I want to do two things. For the last decade or so, I have thought about human machine interfaces completely only in the context of building new technologies like consumer technologies be it the larger computers, the mobile technologies, or routable technologies. I want to bring a couple of insights from those thought process of understanding the human machine interface and what sensor technologies have been developed. I don't want to speak for deep learning here. I think there are a lot of people here who are much more of experts maybe. But I want to bring my perspective on what is the paradigm that shifted with respect to data processing and analytics from deep learning and what its implications are for sensor fusion. Then in my current role I am independent consultant mainly building IoT systems. Many applications but many of them are health and wellness and really want to highlight some issues that I have to really deal with that are going meet the road where we're taking all these sensor technologies and trying to develop solutions, for example, in elder care or in addiction recovery solutions. What really are the gaps and challenges if we are trying to adopt these technologies to a real life solutions. In the end I want to propose a framework or really just throw it out there on very high-level thought process around, is there something about the fact that we have language hierarchy and language that we've all developed that itself can be used to better build sensor fusion framework? With all these multimodal discussions that has happened in the past, I just want to say that multimodal is not a nice-to-have but really maybe should be thought of as a must-have. Because that's just how we process information almost all the time. This is my go-to slide to just show the various ways in which we can think of human machine interfaces of whatever you want to call sensors and actuators from engineering perspective. We have the visual which we talked about a lot, which we heard about a lot today and for very good reason because our visual system consumes a lot of bandwidth and the way the information processing, and I'll give some examples. But there are human visuals and non-human visual sensing as some of the chat that's been going on today mentioned. IR capabilities are almost as good as visual camera capabilities. But are not often considered but could be really useful. Same thing with our audio processing, there are very good miniaturized microphones as many of you who use the technology now. But also that technology is not limited by the human bandwidth that ultrasonic sensors that are just as good that can be leveraged very well. We have a lot of touch-based technologies, and then lot less sophisticated smell and taste. Usually when I present this to the MEMS audience, I highlight the gap. But there's really a lot of technologies that have been built in I would say even five years that have made big leaps in terms of its ability to be used in various settings that you're all talking about, that includes VOCs, alcohol, carbon monoxide, carbon dioxide gases. The same sensors can also be used to measure not just the human reaction but also the environments complexities as the first panel setup. In this context I want to give a few examples to show why, and they are all extracted from this one paper that's quite old more than a decade. By no means anything new. But just want to say that the process audio and vision almost exclusively together. If there's a dissonance between the information coming in our visual channel and audio channel, then we will prioritize what is a very evolutionary concept. For example, they're like already agile studies have shown that if I used to have a video to test it on people. If you have blinking lights at three hertz and audio at six hertz, you will pretty much swear that you saw six blinking lights not three in a given sector. Because we cannot even undo that natural very low time constant fusion that's happening. It's the same thing that a lot to do with how vision and our motor control works. This is a classic experiment. You keep both your hands in front of you, try to move the left little finger and the right thumb. Now, do this and try the same thing. Try to move your left finger or thumb. It's takes longer because we have to undo the visual contradiction before we do this. There's this sensor fusion that's going on at multiple timescales across multiple modes of sensor that we need to be very cognizant of. Especially if you're trying to think about using a human reaction across only one mode as representation of something that's more complex like behavior. Here I'm switching track to say that now that we've miniaturized sensors and we put sensors everywhere, there are a lot of these ideas about models being thrown around. On understanding this large dataset, I just want to highlight a few important considerations to keep in mind. Image, especially visual deep learning, has come a very long ways than a decade. But the whole basis of a lot of the deep learning is these 14 million images that have been hand annotated and they've also been hand taxonomized in terms of hierarchical representation. This is not something that was done without this training data. Then there is this human in the loop. Only thing is the human understanding of the context is removed by making it really simple. It's just one object, one bounding box thing. Wanted to highlight that in many of these models the context is lost while building the model. Then there are sophisticated ideas that are added to build the context back in. That has large language models that are really also gathered lot of momentum. Have all the contexts built-in or because they are not supervised models. But they tend to have other issues because of what is the data that's going in. They can only reflect the context of all the reader that is actually fed into the model. There is not real easy ways to understand how to validate the models independent of the data because they are just fully built-in together. Having said this, just want to also say that maybe there are some very critical learnings from these models success and some of them are around. For example, if you think about medical sensors, there is lot of questions about how accurate is a simple variable device and just even being able to measure heart rate especially around variables that are not taken into account like gender and skin tone and BMI. We've shown, for example, in my lab that by simply adding one context variable and activity context to the heart-rate sensors, prediction of a heart rate from the raw optical signal, we can improve that accuracies quite a bit. This is the idea of adding contexts how it can make models be more responsive. But at the same time, also I want to point out that still there is systematic variation and accuracy with variables that are not taken into account in these deep models. We need to be aware of all this if you're building these models that will then be used in real applications on a large diverse population. I want to end this with a proposal or a question more like is that to naturally build a framework to model multiple sensor fusion doesn't make sense to actually take clues from these large language models that have built-in temporal hierarchy and contexts being written around understanding? For example, this is purely schematic. These are not real data, this is just some hand-drawn riddles, but ideas that can be think of general framework where you start with a very low level sensor. Understanding that then goes across multiple timescales, so you build from an alphabet to a word, to a phrase and sentence. Is their ideas here that we can learn from the large language models that we can then build domain-specific models to understand sense of fusion in your particular domain? With that question, I will just open to [inaudible 03:04:43]

Speaker 5: Thanks very much Raji. Now we're switching over to the discussion portion and we have three discussants, Peter Hartwell, Bob Datta and Andre Green. In principle, you each have nine minutes, but as you saw with the previous discussion of the previous panel, it was very lively by people timing in. I'm going to give it to you first Peter and I'd let you then hand on to the subsequent discussants, so we have a wonderfully rich discussion.

Peter Hartwell: I'll see if I can keep it going and thank you [inaudible 03:05:20]. My name is Peter Hartwell. I am CTO, that's my title. I look at this from a very different way. In fact, I've really enjoyed today, the discussion and let me see that I'm out of my elements. I'm going to see if I can actually try to get some of my questions answered. Maybe that's going to help all the folks that are online. In particular, I've been a lean a little bit back Panel 1 and try to tie it together with Panel 2 as I get this going. Because we've seen a lot of other study of disease in humans and then the study of mechanics and animals and I actually approached the behavior of humans for frankly profit, that's my job. In fact, a lot of what I do in this space is driven by my customers which are trying to get some electronic field where they've actually gotten pretty good if you think about the big guys who all those apps that you use and those devices you carry around. Understanding and driving your behavior to keep you on that app or to get you to go buy something or look at something. They're doing that by monitoring your sense or your behavior. The way you type or you swipe or you pause on a screen on your device, is actually monitoring your behavior. That's what I do. I provide the sensors that they go into that very much, let's say Raji gave just right before me and I [inaudible 03:06:49] intro into how silicon and sensors and electronics drive that. It's things that you hold, it's things that you wear, it's things that you carry around. I think Malcolm, I want to actually start with you because you brought up a very interesting point at the end which was, how can we look more across the field? I would have put on this slide real quick and upload then I'll ask you to get rid of it. It's my language. They speak a different language than you all. We call it sensor fusion, which Raji call them multimodality. But it's hardly pulling stuff from different areas and try to get to the root of what is someone doing, about to do, wanted to do, that was where we apply the learning into that. We call it activity classification. The context detection of where is the environment, where are you at and how is that influencing you. Our goal is that you're sitting in a restaurant and your phone doesn't ring, it only vibrates. That's understanding the context of where you are and change the behavior of the device. I just want to show that slide because when I first got asked to join this, I was like, I don't know anything about behavior and then realized actually all I do is try to understand what humans are doing with electronics. [inaudible 03:08:07] you can go ahead and give her the slides. Malcolm let me just touch a little bit on how do we go broader. In fact, I'm looking at the panelists here and a lot of you all are at universities and there's nobody here from my customer's space. That means

Malcolm MacIver: One thing I think about for you is, do you do Ethology on humans? You noted that there are all these contexts to interruptions that our devices hijack our brains with. It would be nice to know more about that, some actual ethology. I wonder if you guys think about that, collecting careful behavioral data and then approaching it from that angle. That's one thought I have going directly of what you said about going broader. But the other thing I thought of it's really interesting that you're thinking as Raji also mentioned. Thinking a lot about fusion and the brain uses fusion across modalities to do essentially noise rejection in a way and that if there's a part of space that is just making a sound but not moving versus a part of space that is not only making a sound but also moving. That can be the mark of the living and that can be the mark of something that is actually a danger or an opportunity. We've known for decades in Neuroscience that there are cells in the superior colliculus and other parts of the midbrain which are really excited by that conjunction of stimuli. It seems like you're coming to the same conclusion.

Peter Hartwell: It is, yeah. But we're driven by a different motivation and may not want to use this to spin it back to Ben. A video is too power-intensive for almost everything that we do. The sole exception right now is that if you buy the most popular VR headset, it's tracking the room with four cameras on it. Again, about two hours in the metaverse before you have to unplug and recharge [inaudible 03:10:26]. But then it's looking at [inaudible 03:10:31] so heavily into video, 62 cameras to track a monkey. I haven't gotten the power to do that so that's where we're refusing other things that Raji did a nice intro for all the different sensors but do you have anything beyond cameras that you're using in the monkey lab?

Ben Hayden: The monkey lab, right now we're just doing cameras. We also have a nice microphone and we've been trying to use that to improve our reconstructions. But so far we haven't really had any success with that. But we really have our hands full with that. I want to say we use these very high number of cameras because we have to dissolve our problems because our species moves around in a really complicated way, in three-dimensions and jumps around and contorts and twists its body. We would use less if we can get away with it. But I think even with one camera you can get a lot of stuff and you can do a lot of really good science. I'm not a chauvinist who thinks that this is, I think it's all interesting.

Peter Hartwell: Galit, you're the one that had wearables that one on your pig. That's a lot closer to my world. We track my magic ring and my wife's wearables like that. Do you find being able to fuse or synchronize between cameras and strap on sensors is a hard problem or is it something you guys have attracted?

Dr. Galit Pelled: We are trying to do that. We have the wearable and we have the videos and we are actually videoing the animals 24/7. We gathered just a huge amount of data that is just unreasonable for students to sit and analyze. We're always on the lookout for AI and new types of technologies. How we synchronize the videos with the wearables. So far we are not where we wanted to be. But this is something that we're looking to do. Actually, here in this panel, there's so much good ideas.

Peter Hartwell: Yeah, I know. There is two, I'm going to run out of time here and so I'll pass it off in a second here. I would love to ask that question about, do you have too much data or not? But I'm going to switch, the one I actually want to ask is, and I'll tie in a personal experience here, is about five years ago my kids were four and six. I put a GoPro on their head and send them out to go sliding up in the mountains here, I'm on a day. We got 60 refresh now. For the first two minutes, my son was like, "Hey, check out at the GoPro, they'll give you the GoPro." They forgot about it, and it is the most enduring video I have of my kids where there was 10 minutes of brother with brother against the world. As soon as I walked up at the end of the video, the older one push the younger one out of this snow. They were this team when I wasn't observing and they forgot about the observing. My question is, it may be in the animal world, it's not as you're influencing the behavior by observing it. But I wonder if the human world, particularly in the VR thing I was thinking about as you're running through the fake rat maze, are you really afraid of this big zombie or not? Are we influencing behavior just by the act of trying to measure it?

Malcolm MacIver: I can speak to that last bit. I mean, you're talking about the differences in incentive structures between the rodent and the human work. It's something we're thinking hard about. How to measure the aversive strength of an air puff, which is clearly unpleasant for an animal. But we're basically trying to model predator-prey sequences here and it's clearly not as aversive as possible death. In the context of VR, what we're doing with the ghost is it's a stand-in for what the real penalty is. They're getting paid as subjects and their pay is according to how well they dodge the ghosts.

Peter Hartwell: Perfect.

Malcolm MacIver: That's our way of trying to line up incentives. We can't in the context of human work, have electroshock collar. I'd love that.

Peter Hartwell: But I think I've been thinking back to the back to where I started, which is the gamification of behavior for profits and that's there. I think so, but to answer your question, there is a whole overlap between this world and maybe it's what's going on in space right now. That we actually need to look at the model and how these two worlds can come together. I think really advanced, which you're all trying to do. Anyway, somebody pass it on to Rob Datta here. I'm letting you take around 2.

Sandeep Robert Datta: Great, thanks. I'm Bob Datta. I'm at Harvard Medical School. Maybe just to follow up on a little bit of what Peterson has made a quick comment before proposing my first question. I think it's interesting. We've heard a lot about sensor fusion in this block of talks. I think it's worth noting that there's probably a deep relationship between the problems that engineers are solving when they're addressing challenges related to sensor fusion, and the challenges that neurobiologists, ethologists face in trying to understand relationships between high-density neural recordings and high-density behavioral recordings. In both cases, I'm trying to fuse very dense data streams that are time-varying, and you're trying to both dimensionally reduce things and to infer causal relationships between things. I suspect there's a very active dialogue that one could imagine between the people who are building tools for understanding neural behavioral relationships, many of them are on this call and those who are more out in the real world trying to solve complex sensor fusion problems. Anyway, that's just a theme that I noticed in this session. Obviously, the session included a lot of very different perspectives, ranging from thinking about new model organisms to thinking about evolution and engineering and sensors. I was thinking hard about what question might unify all of these perspectives. I realized that some of what Ian said, I think might be very relevant here, and so I'd like to start by posing a question to Malcolm. Raji and Peter both talked about sensors, the importance of sensors and sensor fusion and Malcolm, Ben, and Galit all talked about behavior largely from the perspective of movement. But as Ian brought up in his top, a lot of movement is really about moving sensors around. It's a closed loop between behavior and sensation in which it's not so much that behavior is necessarily the output of the brain as it is. Behavior governs the inputs into the brain. My question for you Malcolm and then to everyone else is, if we're going to understand behavior, how important is it for us to ultimately gain access to information about what biological sensors are sensing during behavior? Is part of the game here not just to measure behavior, but also to understand what the eyes are seeing and what the ears are hearing? From my perspective what the nose is smelling. I'll just let you reflect on that.

Malcolm MacIver: Yeah. Well, thanks for the question. I know it's a tough job of synthesizing across these talks. But this is a great question. I would say, the perspective of behavior being the body's way of getting sensors in the right position is bang on. Indeed, I feel like one of the big advantages of the synthetic approach with simulating the whole organism in its environment is the opportunity once you actually have good high-res 3D data on where an animal is in space to reconstruct what sensors are getting at the receptor level in a careful way and use that. What's nice about that is, you're not going to get it exactly right because there's a lot of nuance there. But what's been super helpful in terms of the earlier part of the work that I talked about in my bit is that once you've done that that leg work on what's happening in this crazy complicated condition that isn't feasible for busting neural circuits is that you can take what you gain from that synthetic approach and then put it into the animal in a context where you can do the more reductive forms of neuroscience that sometimes need to be done. It's not always convenient to do freely recordings in animals. Sometimes you need two photons with head fixed for example. But having the recipe for the signal from the synthetic approach I think is all important in terms of getting the circuits to behave in the way that's maximally informative for subsequent interpretation. I think it's a really good point. Thanks for the question.

Speaker 22: It's not the only thing though. Behavior is not just about getting better information. The real goal of behavior is rewards and survival.

Malcolm MacIver: Yeah.

Speaker 23: I'm sorry, I just wanted to add that, we can talk about sensors, streams, but in animals, those are really dependent on the context themselves. We heard there's autonomic receptors on muscle spindles, there's motor commands that go to them, to your eyes and your ears. It's really hard to think about the sensors being decoupled from any of those other states that we've talked about. We need to recognize that.

Malcolm MacIver: That's a good point. Absolutely.

Sandeep Robert Datta: In a sense, thinking about getting access to sensors is premised on getting some access to internal state.

Malcolm MacIver: Yeah, convenience of the electric sensory system. But you don't have it in many other systems.

Peter Hartwell: Yes.

Malcolm MacIver: There is a lack of efferent control on the afferents. But subsequent to the first, second, third order of neurons, all kinds of state information comes into play. Absolutely true.

Peter Hartwell: Ben, so I wonder what you think about this. I mean, the areas and the brand that you're recording contains sensory information, motor information, and as you were mentioning reward information, how are you thinking about relating all of those different types of information to the ongoing behavior in the monkeys that are recording?

Sandeep Robert Datta: Can you say that again?

Peter Hartwell: I was asking, you're recording in these frontal areas in the monkey, which encode admixtures of sensory and motor and reward information, as you were mentioning before, and I was wondering how you were thinking about understanding those signals in the context of it's really complicated and naturalistic behaviors where monkeys are running around.

Sandeep Robert Datta: Yeah, I mean, I think the highest level the answer is the old-fashioned way of looking at it that I've been doing for 20 years is like, what did these neurons represent? That whole approach really isn't working very well. It's not really driving us towards answers. It has this compound problem, but I don't even think it's a good description of what the neurons are doing. One thing that we're doing right now is we're basically dismantled at a starting all over. We're saying, what can we say about these neurons? We can start with saying, well, to some extent, even neurons throughout the people in the cortex seem to be having a role in controlling behavior. That's something that we can say with confidence. We're doing as far as we can with that and saying, well, what else did they do besides that or what else do they do besides indirectly controlling behavior or setting the stage for behavior. I think that's going to wind up explaining almost all the variance of the neurons. That's just a prediction though. I guess I have one last question, which is something that I think was touched on a little bit in the first panel. I think it's a very broad and general challenge for all of us, those of us who are density measuring behavior, which is given dense measurements of behavior. How do we assign meaning to movements? I mean, many of the speakers in this panel are making high dimensional, dense recordings of various aspects of behavior, some in very unconventional organisms, right?

Speaker 8: I am so sorry this is Dana and I really don't want to interrupt you because this has been so fascinating, but I want to make sure Andre has a time to at least give his thoughts as [inaudible 03:23:46].

Sandeep Robert Datta: Please go ahead then.

Speaker 5: Dana. He will get his time. We started late, so we will run a little bit late. I don't know if Bob, you've got I'll just.

Sandeep Robert Datta: Let's quickly finish this question that we can definitely move on. Which is just, I think lots of us are piling up these high-dimensional descriptions of behavior. It's not always clear how to understand what the data mean in the sense that movement and behavior aren't synonymous. That as Lena was mentioned in her talk. For those of you, especially [inaudible 03:24:24] who were looking at animals like octopus or pigs for which there isn't a huge amount of behavioral data that we can center our thinking around. How are you thinking about assigning meaning to the various high-dimensional movements that you're observing?

Lena Ting: I didn't show. For the octopus for example, we are interested in a very specific movement, which is the grasping movement. We actually train the octopus to grasp. It is intentionally executing a very specific motion. We don't have everything that happens in the tank, of course, in the future, we would like to sample all that simultaneously. But we do feel that we have the intention of the movement.

Speaker 8: Would you mind your camera and jumping into the conversation because I really want to hear what you have to say and we will give you the time and platform to speak and we will cancel the break.

Speaker 5: Thank you. Dana his camera is, he spent [inaudible 03:25:39] following the discussion. So thank you. Andre

Andre Green: I appreciate it. Thank you. Actually, I might maybe a relatively quick, but I think one thing that I've heard across all of the toxin, including the ones in this panel. This tension between working in controlled environments where we can have a much maybe tighter understanding of a particular process that we're looking at versus what we all want to get to is the natural environment. How are things behaving in the natural environment? What I guess I've been thinking a lot about in terms of working with the monarchs, because I'm interested in monarch migration. How are they using multisensory cues in order to navigate? Why do they go to specific places which such incredible regularity? Whenever I start my own experiments, we can use the usual environmental cues, the usual suspects. I'm not able to recapitulate some of the phenotypes and behaviors that I'm interested in. It made me take a step back and ask, well, how would I in an unbiased way, determine what is environmentally relevant to the phenotype and I'm looking at? Honestly, I still don't have a great answer for that. But I'm thinking about Peter and Reggie who are thinking about multi-modal fusion. We've already made this realization that of course, in that natural environment that we want to understand behavior. This is what more recapitulates what's actually happening. For the folks who were in the panel, how do you determine for your own work? What in the environment is important? What do you tell the people that you asked to work with? With the sensors? What should they be measuring? How do you guide them through that?

Malcolm MacIver: I'll take a stab at answering that. I would love to be at the stage. You're thinking about your system with, right. At the present time, all the experiments we do with animals are fairly constrained. Minus the new work where we have these complex habitats with rodents running around with robots chasing them. That's pretty unconstrained but the earlier sensory work we did, a lot of it, a lot of the analysis we've done is situations where there's one object to track or something like that where we really try to simplify the situation so that there isn't a lot of ambiguity as to what is going on. I will say one thing that's emerged from the analysis across a bunch of species, this is work we published last year in E life. So we analyze some data from hawk moths, from electric fish, from cockroaches, and type of rodent or type of mole. Is that there is an information theoretic a way to get at what you're saying. That is from an information theory perspective, when an animal is encountering something that has a rich amount of information in the space. There is some characteristic behavioral changes that we documented in that paper, including reducing velocity is something that is very characteristic of entering a high density space of information for an animal. Another thing is there's a frequency change in the way they move their sensors. There's a date start inhabiting a different region of the Fourier space when you do an analysis and frequency space, once the sensors are activated and when they're not in a high information zone, it changes to acquire less information. I think there might actually be some information theoretic tools that can start to help with the problem that you're tackling, which is not a problem I'm yet tackling, but I think I will be meeting too soon.

Speaker 5: I think that's a really interesting way to think about it, Malcolm, because the way that we do it as that, or in clinically is there's a behavior, as I was talking about freezing of gait and we never capture it. It's always like after the trial is over than the patient turns. Then it happens when we actually catch it. It's like, Oh my God, we keep recording. Go back into this more real type of behavior. We were actually struggling with what are the things that we need to control in the lab to actually get the behaviors that matter. I think distraction and high complexity of environments is really important. Of course again, I think this came up anytime somebody walks into our lab, It's just they want to make sure that they're doing it okay. Unless they're college students, they just want their money to go. The context we realized that when a patient comes in versus when a college student come in, it's really, really different to if they're motivational for even being there.

Malcolm MacIver: I think one crankshaft when we think about trying to wake up your phone, if it's sitting on the desk actually know you're not holding it, it goes into a deep sleep state. If I pick it up and I know you're holding it, that's another one. Then if I know you're actually looking at it, or I also listened for audio cues and see if there's anybody in the room. We actually build that hierarchy into the electrical system. You trigger me Malcolm, to think about for us that the currency is power. We're trying to improve your user experience by making your battery lasts all day. Then they can devise leads warm, but mainly I'm actually synthesized and how your organism is dealing with various levels of sensory input. We're actually building those models and will evolving to quote somebody earlier today.

Dr. Galit Pelled: Yeah, I think there's also a little bit of context around the impedance mismatch and behavior of change that you can do. That is the cost like an auxiliary costs like power, for which you can optimize if you're doing system-level thinking and one time design. But as a continuous evolutionary use, 10 years ago or 15 years ago, how many of you would have done this? You're waiting an intersection and you just snap a photo of the two signboards to send to your friend where you are. That picture is not worth a thousand words. That picture is just worth two words but it was just has lower impedance to use. Some of these behaviors of which sensor you choose. Then might be not purely about system design, but also context. That particular cost at that particular, more local. I think there are multiple timescales and things that you should consider rather than purely about. That's what's interesting as someone who had to choose between biology and computer science. Very early in life in 11th grade, which I was at the most disastrous day in my life. Learning about all these animal models, which I don't get a chance professionally to ever encounter is very fascinating because I think given a chance I might have studied octopus and generic.

Speaker 5: Andre, did you have other questions for the group?

Andre Green: I think many of my questions were definitely covered over both of the sessions. I appreciated hearing these perspective and also I mentioned here this thought of constructing virtual environments and analyzing behavior in that way paired with this question of what the environment is important. It triggered the really peering those two. Now I guess I'm going to be thinking about that for the rest of the day, so I really appreciate all of the comments here.

Speaker 5: Thank you. Terrific discussion. Things that I noticed, really as just mentioned, so that the different temporal scales and spatial scales, both with respect to the organism, what could be measured in and around, if you wish, on the organism. But also with respect to the context and context, there are many ways of interpreting contexts. Again, it has different spatial and temporal scales. The problem of not only what data is collected, but how to fuse the data streams and the synchronization across those data streams. Then something that came up, interesting comment about the effect of the observer. As we for instance, constructed environments, as we construct means of measuring, are we actually altering what we want to capture? With that, those words, we're going to skip the break and move over to the third panel, Ming I hand it over to you. Thank you to all the panelists and speakers.

Dr. Ming Zhan: Thanks so much, that's a terrific discussion and presentation. Now let's move on to the Panel 3. I am Ming Zhan, Program Officer from National Institute of Mental Health and Brain Initiative, and I will be moderator of this product workshop. But the title of this Panel 3 is from data models and the back. The meeting will be focused on overreaching questions, that is, what are the capture additional opportunities and the challenges for modeling behavior environment as our complex and a dynamical system. We are pleased to have a list of distinguished panelists as a list on this slide for this meeting. This includes a full speakers who are going to give full presentations to this panel. Dr. Dani Bassett from University of Pennsylvania, Dr. Scott Linderman from Stanford University, Dr. Maryam Shanechi from University of Southern California, and Dr. Gordon Furman from Emory University. We also have a three discuss who are going to lead panel discussion after the presentations. Dr. Allison Waters from Icahn School of Medicine, Dr. Tayo Obatusin from Icahn School of Medicine as well, and Dr. Tim Brown from the University of Washington. Each presentation going to be short about eight minutes of time. For the presenters please be mindful of your time during your presentation so we have enough time at the end for discussion and question. We are not going to take questions or comment during or at the end of a each of representation, but we will take questions and comments during the panel discussion phase after all four presentations are complete. Let's move on to the first presentation by Dr. Bassett. Dr. Bassett, please takeaway.

Dr. Dani Bassett: Thank you so much for the opportunity to be part of this workshop. I'm really excited about the topics that have been raised this far, and excited to provide you with a little bit of an overview for this particular panel. What the organizers asked me to do in this panel is to talk quite broadly about how we can think about behavior as a complex system. Then in the next three talks, my colleagues will be digging deeply into specific instances of this general idea. You can see mine as a broad overview talk and then we'll move down into more specifics. First, I would say that I'm going to be providing this overview from the perspective of cognitive neuroscience, which is one of the areas in which I work. In that field the typical view of behavior, is that the brain causes behavior which then produces a change in our environments. What's interesting about this approach is that it foregrounds a relatively simple one directional causal structure. The brain drives behavior in a one-dimensional line, and behavior then drives something in the environment. An example of this would be a study that shows that the lateral prefrontal cortex drives a particular reaction time, and that makes an impact on the environment with a keyboard press. This is a typical set of units of information and their relationships that we would view as a good study of behavior in cognitive neuroscience. But I think the challenge that many of us are facing is that, of course, behavior is not monetary nor related to brain and environment in this symbol, unidirectional causal structure. First, I want you to focus on the left-hand side of this slide, and the point that behavior is not unitary. Instead of having one blob that is behavior or in cognitive neuroscience very often reaction time, in fact, we have many behavioral bits. For example, a micro movement, or an eye twitch, or a non-verbal sound, or a tightening or relaxation of the muscles. Those behavioral bits display statistical and causal dependencies upon one another. Really we need to think beyond the unitary description of behavior. But secondly, the second challenge is that behavior is not related to brain and environment in this simple causal chain. In fact, what's happening is much more complicated where various pieces of this broader system interact with one another in both feed-forward and feedback directions. For example, long-term behaviors can change the brain by altering input. The environment can alter the brain through perception without action, and the environment can drive behavior through structuring constraints. The picture is really much more complicated than the simple linear three-point box and arrow diagrams. Now I'd like to put these two challenges together. The fact that behavior is not unitary and there's not a simple causal chain. If we put those two pieces together, then what we have is something that's much more complicated. We know that the brain is composed of units, so individual brain regions that are interacting with one another in a complicated way. Their interactions are drivers from each pieces of the brain to a particular behavioral bit, and behavioral bits are dependent on one another. Then the third instance is the environment. Again, the environment is not one thing, it's many things that are interacting with one another in a complicated way. In this broader picture, multiple units exist and interact in each of the subsystems, but more than that, single units or small groups of units can interact between subsystems. Now, we could ask, are we done when we have brain behavior and environment in this broader structure? I think that many of us in the field would say no, of course we're not done, the brain is not necessarily the first cause always in an Aristotelian sense. Maybe we need to press further back to understand processes in the mind, like beliefs, desires, intentions, and purposes that may not produce action except by going fresh through the brain. Understanding behavior, I think, requires us to reckon with the psychological processes involved. Understand their map to the brain network, and then the map to the behavioral network and environment by extension. I think having these four pieces in mind is important when we think about a single organism. Of course, the piece of the picture that I have not added in here is when you have multiple organisms interacting with one another in social systems or other collectives. But I want to dig a little bit deeper and say, are we done? The answer I think is not quite. Because each of these interactions, both within and across systems can change in time. Within the mind individual mental processes have time-varying architectures. The brain at regions have time-varying interactions. The relationships between each of these subsystems have time-varying interactions. Every link inside of this picture I placed a T on, because they are time-varying. They are not static, and the change in one piece, can alter the change throughout the entire system. More than that, one layer even further is that each of these units can have associated timescales. Timescales of activity in the brain, timescales of action and behavior, timescales of strengthening or weakening of mental processes in the mind. I've placed a tau in every single unit now, both within a subsystem and then for each subsystem itself. What is this, this picture that I'm showing you now? This picture is a picture of a complex system. It is a system that is composed of many individual units that interact with one another and complicated time varying ways to produce very sophisticated phenomenon that occur across all of the subsystems. Understanding this complex system requires us to bring complex systems tools to the table. Tools meaning algorithms, meaning conceptual frameworks, meaning theories, meaning computational models. Of course you could be sitting in the audience thinking, but hang on everything in science is really complicated and we can say this about anything that we studied, but isn't the point of science to try to simplify things down, to make some simplifying assumptions and then focus in on the very individual parts and how they might interact with one another. Could I take that broad complex system I just showed you and map it down into these four units and this simple unidirectional causal structure. The answer is not quite, not if the timescales of the parts matter for how the system function. Those were the towels in the previous slide. Not if the temporal variability of interactions matters for how the system functions and that was the individual T on the previous slide. Also not if the pattern of interactions matters for how the system functions. If timescales, temporal variability, and patterns of interactions matter for how the system functions, then we can't really get away with this simplified picture. But you could also say hang on again, if we don't have this simple chain, that I'm showing you on the left-hand side, then how do we know when we built a rigorous explanation? What explanations are even possible, which are causal and which are not causal. On the left-hand side, what I'm showing you is that the relevant causal concepts here can be relatively straightforward. A simple causal dependency between two units. Whereas when we have-.

Dr. Ming Zhan: Hi Dani you have one-minute remain. Sorry.

Dr. Dani Bassett: Thank you. Whereas when we have the complex system that you see over here on the right-hand side, there can be many relevant causal concepts. The first is a simple causal dependency, the second is a structuring cause, so how the structure of the interactions may cause particular dynamical processes, triggering causes, pathways, mechanisms and cascades. I wanted to raise these ideas because there's some really beautiful work in the area of philosophy of science that focuses on understanding diverse causal concepts that may be very helpful for us in understanding complex systems. This is my last slide, which is what I think of as paths to progress. The first is to prove interactions within and between these subsystems, to map the timescales of parts, to examine the temporal variability of interactions, and lastly, to expand our understanding of diverse causal concepts and use them to develop more precise hypotheses that hue closer to the nature of this complex system. With that, I'll end and see the floor to my colleagues. Thank you.

Dr. Ming Zhan: Thanks so much, Dani. Excellent presentation, and I'm going to kickoff for this panel. Now we move on to the next representation by Dr. Linderman. Dr. Linderman takeaway.

Dr. Scott Linderman: Great. I am still waiting for the controls there we go. Excellent is great to be here. I am an Assistant Professor in the Statistics Department. I am a computational and systems and statistical neuroscientists. What that means is that I developed models and algorithms to try to understand and glean insight into large-scale neural and behavioral datasets. The topics of today's discussion are very near and dear to my heart. As I was preparing my talk for today, I was looking at the title of this panel and realizing that an equally appropriate title would be to just call this Machine Learning and Statistics. Because really going from data to models and back is essentially what the fields of Machine Learning and statistics aim to do. Aim to build models of large-scale datasets and use those to make predictions, to draw inferences and to make decisions. What I'd like to do today is to talk a little bit about how ideas in these fields are contributing and how they can continue to contribute to advances in the analysis of Maryland behavioral data. As I'm sure you've seen, the buzz around machine learning has permeated the popular press and some of this excitement is hype, but a lot of it is for good reason. Things like OpenAI's GPT-3 language models can write essays that are so real that you might think that human wrote them. Netflix made a documentary about DeepMind's AlphaGo system, which probably years ago beat the world champion in the Game of Go. These two technologies have started to make a real big impact on science as well. A team here at Stanford used some deep neural networks to make predictions about RNA structure and DeepMind very recently used deep reinforcement learning algorithms like those in AlphaGo to control plasma in a tokamak, which is an important step towards sustainable energy based on nuclear fusion. What are the key ideas or some of the key advances behind these accomplishments. One of them is, availability of very large-scale datasets so GPT-3, the language model, is trained on an Internet scale corpus of texts. In the plasma control problem where real data is very expensive DeepMind used very detailed physics simulators to generate massive datasets. The second ingredient is advances in algorithms. Many of these very large scale datasets are unlabeled like those that we collect as part of this field. One of the trends towards taking advantage of large-scale unlabeled datasets is towards self-supervised learning in which we come up with synthetic prediction problems like filling in the missing word in the sentence and then using those prediction problems to train large-scale models. Third is, of course, hardware, so we are familiar with GPUs which have powered this Machine Learning revolution. There's more advances in that domain as well. The fourth is in the architectures, the models that we actually build for these data. Deep neural networks, which have come up multiple times today, which have hundreds of billions of parameters in some cases, lend themselves to massively parallel computation. An interesting observation is that the structure of these architectures may not matter quite so much as their flexibility given satellites amounts of data. Pivoting now, how can we take advantage of some of these advances in machine learning and apply them to problems in brain and behavioral quantification? Well, to answer this question, I think that it might be helpful to try to categorize the types of problems that we encounter. The categories that I'm showing here, these four are certainly course and incomplete, but I think this might be a useful first-pass for organizing our thinking. The first is one that we've already seen, signal extraction. How do we get signals of interest from raw neural or behavioral video posts? Extraction is an obvious example, which we'll talk about shortly. The second category has to do with building encoding and decoding models. How can we predict neural activity given behavior as the encoding side, and vice versa, how can we predict behavior given neural measurements? That's the decoding side. These problems have obvious importance to the development of brain machine interfaces and to establishing the underlying neural basis of behavior. But on the translational end of the spectrum, these are also important tools for discovering biomarkers of disease. Third category is toward generative modeling of neural and/or behavioral data models that can simulate and reproduce patterns that we see in these massive datasets. Why is this useful? Well, generative models are often built from latent variables that are much lower-dimensional than the raw data and these are useful for both dimensionality reduction and visualization, but also for some of the topics that have come up about internal state estimation, which is certainly an important aspect of this talk, as is inter-subject variability. Fourth and finally many of the advances in Machine Learning have targeted problems of decision-making and control. How can those start to feed back into the analysis of neural and behavioral data? I think one example is toward guiding Optogenetics stimulation to aid us in circuit busting to most effectively established causal relationships between neural activity and behavior. Again, more on the translational side the same types of ideas can be used to develop deep brain stimulation or TMS therapies like what we've seen earlier in today's sessions to try to individualize our treatments for each patient and counteract different types of diseases and disorders. Today what I'd like to do is highlight some recent work from the community, which is pointing to and showing some of the opportunities of the advances in these different domains. Digging in, starting with signal extraction, this is perhaps, maybe the clearest of the four, and I think one that we've already seen a few examples of. You've heard about methods like deep lab cuts, sleep, and dance a couple of times today, these are tools that allow us to track points of interests and raw video. Points of interest on an animal's body is that animal freely navigates its environment. Why is this a good showcase of advances in Machine Learning contributing to behavioral analysis? Well, one popular approach to solving this problem is to take a pre-trained neural network, a so-called foundation model as some are calling them, which has been trained on a massive dataset of images, but not necessarily for this particular task. Then to use what we call transfer learning to adapt that network to the problem of post tracking. This has shown tremendous improvements in our ability and as you can see from some of these examples from say sleep here in the middle, highly accurate abilities to track points of interests. But where do we go next? Certainly the skeletonization is a highly compressed version of the animal's behavior. One trend that I'm seeing that I think is really important and exciting is toward a more comprehensive quantification of behavioral state beyond just key points of interest in toward fine-grained measurement of oral facial features or as you see in the bottom right, towards mapping of the whole surface, a shape of an animal's body. These are just the tip of the sphere they think is pointing to some of the possibilities in this domain. Moving on to encoding and decoding. Decoding is the problem of inferring behavioral outputs from neural measurements. One application of this is in the area of developing brain-computer interfaces. Here I'll highlight a piece of work from Frank Willett and Krishna Shenoy and Jaimie Henderson's labs here at Stanford. They developed a brain-computer interface for decoding handwritten characters. They have an implanted Utah Array measuring neural activity in an area of motor cortex, and they're using that measured activity to guide a handwriting.

Dr. Ming Zhan: Just a minute, Scott. You have one minute remaining.

Dr. Scott Linderman: Well, I'll speed this up considerably. Where do we go from here? I think they've shown this for handwriting, but the same strategy applies to other behaviors, like decoding much higher-dimensional behavioral outputs, muscle activity, speech, etc. The key aspect of this is building good generative models for those types of time series much more than the language models that they used in this example. Third example of generative modeling, I've already told you a bit about how these tools allow us to get low-dimensional representations of neural activity. One nice example comes from Eva Dyer's lab where she's developing models to disentangle content from style of behavior, which direction from which velocity, etc. They're using methods like variational autoencoders and coming up with very creative ideas to apply self-supervised learning ideas to this domain as well. I think here, again, there's tons of room for improvement as we continue to push this forward. This is an area where my lab in particular is excited about the possibilities for developing better generative models for behavior. I think we have the ingredients necessary to do so. I'll skip this last example just to briefly and only briefly mention it. As I said, the fourth area where I think ML can really stand to contribute is in this online and closed-loop control of neural and behavioral systems. One example is in closed loop deep brain stimulation here for major depressive disorder, highlighting work from Catherine [inaudible 03:57:05] who's leading a breakout session tomorrow. Once again, I think that this is an area where ML stands to give us much more comprehensive behavioral summaries than just the patient reported symptom scales that are currently used. Our collaborators in the battle lab at Harvard have shown how motion sequencing technologies can get very rich descriptions of behavior. These are clear candidates for developing better biomarkers of disease, which you can target with reinforcement learning algorithms for control. This is four areas. This is my attempt to try to organize our thoughts about where we can and how we can apply advances in that manner to the development of better technologies for brain and behavioral modeling and quantification. They're not complete. One thing that's notably missing here is any theory building. Certainly, I think that falls under this umbrella of generative modeling as well to some extent, but also deserves its own place on the podium. I'll leave it at that. I'm looking forward to more of the discussion with the other panelists.

Dr. Ming Zhan: Thanks so much, Scott. Wonderful talk. Then we move on to the next presentation by Dr. Shanechi.

Dr. Maryam Shanechi: Thanks very much. Pleasure to be here today and talk about some of our ideas on joint modeling and behavior on neural activity. In particular, I'll talk about data-driven dynamical modeling of these signals together that can both benefit basic neuroscience investigations as well as neural technologies for decoding and modulation of abnormal brain states. As you know, there has been significant work in progress in recent years on dynamic modeling of high-dimensional neural activity and modeling these in terms of low-dimensional latent brain states and then the temporal dynamics within these brain states. For example, here, showing how the brain state goes from one time to the next time step. I'm showing this in linear form, but there's, of course, also a non-linear deep learning approaches to build these types of dynamic models. The goal of these models has largely been to describe as much variance in neural activity as possible. But of course, in a lot of applications questions, you're interested in the neural states that are behaviorally relevant on how neural activity relates to a specific behavior of interest, let's say arm movements. In this case, then we want to extract those latent states that are shared between neural activity and behavior. Now, if you think about these states, we can decompose them into three components. Those that are just in neural activity, which are those red things, those that are shared, which are those green ones, and then the blue ones that are just in behavior. If you use unsupervised methods that just consider behavior or neural activity, what happens to what the extract using these ML approaches? First, if you are unsupervised with respect to behavior as a lot of these neural dynamic models are, what can happen is that we may actually extract those red states that while exists in neural activity are not directly relevant to the behavior of interest. Now, there's also representational modeling framework that essentially do the opposite. First, don't look at neural activity, build a dynamic model of behavior. What can happen is that we may actually extract those blue states that while in behavior are not encoded in the particular recordings of your [inaudible 04:00:40] . But there's this potential to come up with joint dynamical modeling and machine learning paradigms for behavior and neural activities simultaneously. We develop one such learning algorithm called preferential subspace identification to extract and dissociate these brain states. I'm going to show you what benefits this can have. Now, the method is essentially a latent state dynamical modeling method that can dissociate these red and green elements based on the idea of projections. More importantly, it can actually prioritize those shared behaviorally relevant states. But to see how this can benefit our modeling of this behavior relevant dynamics, we applied our method in monkey datasets where monkeys were performing a naturalistic reaching, grasping, and return movements, and looked at the explanation of behavior from neural activity and the decoding of behavior. We found that this joint modeling allowed us actually much better equal behavior compared to both representational models and unsupervised dynamical models. Moreover, by dissociating those relevant dynamics, we found that the behaviorally relevant dynamics actually had much lower dimensionality than we would otherwise conclude. The same conclusions held, then we compared with nonlinear deep neural networks, for example, sequential autoencoders. The other application that this joint modeling has is for targeted dimensionality reduction in a dynamic manner. We use this joint model and unsupervised models to visualize a low-dimensional representation of neural activity during the reach and return movements. What we found was that the PSID algorithm, again, by drawing these dissociation, found the rotational patterns that they're more congruent with the fact that movement itself was changing directions. As you can see, these rotations are changing direction, whereas the other rotations are not. If you want to do dimensionality reduction on high dimensional neural data in a manner that ensures we maintain information of our behavior, this joint modeling can be useful. Finally, while I've shown you this linear instantiations, we can think about extending these ideas to the realm of neural networks as well to allow for more complex nonlinear modeling. For example, if you think about building return neural network models where each parameter in the RNN corresponds to one of these interpretable mappings, then we can develop learning algorithms that can again dissociate and prioritize shared dynamics by coming up with cost functions that encourage both not only neural prediction but also behavior prediction. We've done some of this development showing that, again, both the nonlinear modeling and the preferential behavior modeling can improve the description of neural and behavioral data. Finally, these models can be used as tools for science, for example, to decompose these transformation from neural activity to behavior into these mappings and ask where is the nonlinearity, as one example. But we've indeed done this showing that we find a consistent result across multiple behavioral domains that nonlinearity can be, for example, summarized in the mapping from this latent representation to a behavior suggesting some downstream of cortical processing that captures the nonlinearity. What about the application to neural technology? These kind of dynamical models can actually quite a benefit on brain machine interface development, as we already heard from one of the speakers. One of the applications will be BMIs that decode movement, but a second application could actually be for BMI is that it aim to regulate abnormal states, for example, let's say mood in depression. In this case, we want to build these closed loop stimulation systems that can decode in mental states such as mood. Then use that as feedback to adjust the deep brain stimulation parameters to take the brain to a healthy target state. But how could these dynamical model be helpful for building these closed-loop stimulation systems? First, they can be helpful to build a decoder by building a dynamic encoding model of, for example, how mood is represented in neural signal. It can also be important in building input-output models that tell us how stimulation input changes neural activity and therefore the underlying mental state and finally, these models can be incorporated within feedback controllers to adjust the stimulation. What are these datasets modeling?

Dr. Ming Zhan: Hey, Maryam. You have one minute.

Dr. Maryam Shanechi: Sure. For example, when we talk about these mental states such as mood, the observations of these mental state, the behavioral observations are typically in the form of questionnaires that we give to patients. Here I'm showing you equal activity and I show you the questionnaire that we give patients to measure their mood, essentially an iPad based questionnaire. You can see that in the case of these mental states are behavioral measurements they are actually unlike movements, pretty sparse. We have very sparse labels by which we have to train our models and why we've shown with unsupervised methods that we can, for example, decode successfully, there's a lot of potential in using these joint dynamical modeling approaches to significantly improve the quality of decoding. Similarly, for the input-output models from stimulation to neural activity, while we've shown in an unsupervised manner, that we can describe our neural variation in response to stimulation, there's a lot of potential in extending these models to describe a response on just mood relevant neural dynamics, for example, so that we can precisely target just those dynamics while minimizing side effects on other dynamics. But to summarize, there's a lot of potential for building these machine-learning algorithms that can consider jointly behavior, as well as neural activity, both to study the neural basis of behavior, but also to develop next-generation technologies. With that, I'll pass the floor to the next speaker.

Dr. Ming Zhan: Great talk. Excellent thought of algorithm. Thanks so much Maryam.

Dr. Maryam Shanechi: Thank you.

Dr. Ming Zhan: Then we move on to the next and that's a last presentation for the panel. Dr. Berman. Dr. Berman, take away.

Dr. Gordon Berman: Thank you. Thanks for the invitation, and thank you everybody for sticking around to the last talk. I'm going to talk today about a bit more overview talk, thinking about, how can we develop a theory of behavior that allows us to make sense of underlying neural activity and underlying other sorts of structures that we're seeing. When we're talking about behavior, behavior often has this notation of thinking. It's not just the particular actions and the movements in animals. Is making really one of the things that we really care about and I think one of the key aspects of this workshop is thinking about not just the particular movements that an animal is making, but also what are the underlying features that are generating those movements? Then how can we go and use those to make sense out of these things, for example, between the movements an animal as the function of its activity level the circadian rhythm, its hunger, it's age, social interaction with those around us? Of course, this is very important for thinking about clinically relevant things like mood disorders or other types of things that we might be carrying about as we think about humans for this. When I say, there's been a paucity of theory to really think about how do we really understand these internal states of behavior and how this actually winds up relating to those outputs that we're talking about. But there has been a lot of linguistic theory that's going around this. Not literally linguistics, but what I mean by that is beautifully written thoughtful ideas that come from say, for example, the classical ethology works from Tinbergen and Lorenz and [inaudible 04:09:39] and Richard Dawkins and others with 50, 60, 70s, really trying to think about, what might that structure behavior be? That structured behavior, really what it often is, is it's a full repertoire. It's not just one thing an animal is doing, trying to understand this one thing and understand precisely how it's doing it, but also where does that thing fit in the context? Context is the word has come up a lot today. How does that context emerge amongst his whole repertoire of behaviors? The other key factor is thinking about hierarchy of states and a hierarchy of underlying eternal States, and really trying to understand how those things are interacting in time. We can take a look to see. This is some ways relatively simplistic models or even just not case, there's not any math underlying them. If we look at some of them are the beautiful work that other people have done this or this is some great work, including by several people that are here on the panel today, but what we typically see is these types of models for describing behavior that have a tendency to have a relatively short timescale and to be relatively discrete and what we mean about by these internal states. It could be discrete in the standpoint of I am grooming my right ear, now I'm going to groom my left ear. So there's these discrete states and these are discrete stereotype states. There's a lot of great justification as to why that might be a good way to talk about behavior. Or we say, "Okay, I am grooming. I'm coding. I am doing something else," and so then, okay, I'm going to switch between these higher-level states and between things. But that doesn't necessarily map on and this is basically the picture, and I'm sorry for the fonts got translated rigidly between the Mac and the PC. But what we basically see is, we see this picture where as time moves along, our behavioral outputs are essentially a filter.

Dr. Ming Zhan: You'll have one minutes remaining.

Dr. Gordon Berman: I have one minute remaining? Essentially, a filter between what's the internal state and the external state. How can we think about this from the standpoint of how other people have generated models. For this, I'm going to go back to what Malcolm talked about earlier and can go back to the Higgs Boson as we see here in this beautiful form golden signature from the atlas experiment. What theorists do in theoretical particle physics to build these models, there's an underlying theory which in this case involves writing down a bunch of complicated equations. Then you have a phenomenology, and that phenomenology is the thing which brings the theory into the world of the measurable. That factor of being able to go from these theoretical calculations to something you can actually measure in a complicated detector which is 40 stories tall, winds up being a complicated event, and that's how we wind up getting these things. Another type of theory that we see a lot is, say, for example, we have a very simple system where I'm looking at this water and I want to say, calculate what the speed of the wave is going to be and what the amplitude is. If I were a statistician, what I would do is necessarily to say, "Okay," or minimally, this is what modern machine learning is doing, is saying, "I have my height and I have some external variables. I'm going to train them on on a bunch of data. Train a model to accurately predict that. Then what I want to do is correctly output my prediction. Then if I'm able to correct the output of the future than I go in. Then another way of thinking about this is instead of trying to think about it this way, can we isolate relevant variables from our environment that actually wind up being predicted? From that, this is where he started off of original.

Dr. Ming Zhan: Dr. Gordon, sorry about that.

Dr. Gordon Berman: I thought that was a big tick. Basically, what we wind up having is you start off with something which looks like a Navier-Stokes equation, where you have basically imposing types of symmetries on the environment, in this case, conservation of mass and momentum and translational and rotational invariance. Then you say, "Oh, there's some relevant features I'm trying to predict," which is an effect that wavelength and the amplitude of that wave. Then from basically making a set of approximations, I now have a predictive model where I isolated relevant variables. Now, of course, this takes knowing a lot about your system and sometimes this is really complicated. You really can't do it if your system is too complicated like an animal behavior, which is the result of a complicated sequence of development in neural activity, in gene expression, evolution, and everything in between. In physics, we can deal with this a little bit by thinking about what's called a renormalization group for you. I've just showing this here, for example, of looking at a magnet. You can go and say, "Are there all these tiny little spins pointing up and down?" Then I can find course graining variables. I can group these blocks of three spins into one big spin. Then as I keep on doing this coarsening, I eventually find that these are the variables that wind up being relevant for me understanding my system. What might that look like back in behavior? In our group, we think a lot about these things. The picture that we've been working with an emerging is this sort of, you should take this metaphorically, not necessarily have a set of equations, but the idea of imagining like a little ball is rolling through this landscape, where there's some deterministic part of this where it's going. You can imagine have a ball in a well, but there's some noise, which is pushing it around. Each one of these little boundaries might be a stereotype behavior. But then what happens is that this whole thing might shift or move around and that's shifting and moving around review is that of the internal states of the system and how to understand that shifting is really that matter. There's been a lot of work, including some stuff that we've done, including beautiful work by Bret Stevens and Lena's work that you've seen in bio locomotion. Others, looking at, how do you function in one of these states or how do you go between your bio states? How this whole landscape is shifting is really the thing that I think is important for understanding how to build these theoretical models of behavior. Going back to this picture that I showed before, one of the big issues about this is the discreteness. We know this can't be true in really important ways. I'm showing here two beautiful examples from fruit flies. One example from David Anderson's group, where you see that basically by changing the level of activation of, particularly, neural circuit, you can get different types of actions in this quantitative way. Or in these fruit flies, these different species have similar neural circuitry together. But as you wind up increasing the activation in a particular part of the circuit, you get different behaviors which can result in different evolutionary important [inaudible 04:16:56] . The picture that we have in our heads, and this look prettier on my screen before all the fonts got messed up, so sorry. I have one more slide up. This, interacting complicated states, that are pushing and pulling and dynamically interacting with each other, and then the behavior then filters back and everything else. This is getting really towards what Dani was saying in the first talk of the session, thinking about these complicated dynamic feedback loops. Really, where theory probably is going to come in, is understanding how to infer these things in a dynamic rather than a statistical way. Lastly, I'll just add that what we're trying to do and the needs for going from data to models and back, which I have more or less shown here, is we need to have high-quality behavioral data over long time spans. This is where a lot of progress has been made, as we've seen. Really, the key here, and the point I really want to leave with is that what we need to be able to do is think about modeling in theory from the standpoint of phenomenology. How do we write down models and theories that will allow us to make testable predictions. Not only that testable predictions then we'll feed back into our models and theories. This is where, in some ways, I get worried about using the full-throated machine learning type of approaches in a lot of these types of systems because of the idea that what we're trying to do is really bring things to a level where we can understand the ins and outs and the knobs turn within the system. Maybe it's of the arrogance that comes with working in a lot of systems, but I think that at some level, much of this is understandable. The problem is how can we build theories and models where we can really build that type of understanding and [inaudible 04:18:43] .

Dr. Ming Zhan: Thanks so much Gordon. Excellent presentation; lots of things to think about. We have completed all four presentations and we've been doing very well both on presentation and the time. Now we move on to the panel discussion. We're going to have three discussions, each would focus on a single idea or question generated by the presentations. The discussions are also open for questions and the comments from the audience. Just to keep in mind, each panel discussion going to have 9-10 minutes, so be mindful of time. Let's start with the first discussion either by Dr. Allison Waters. Dr. Waters, floor is yours.

Dr. Allison Waters: Well, first thanks, Dani, Scott, Maryam, and Gordon, that just was a whirlwind tour. We really did it from data to models and back just as we are mandated. We could talk about so many things now. I see that we're poised to discuss a little bit about application. We could go in lots of directions, but I think maybe I'll represent my groups mandate here at the Nash Family Center for Advanced Circuit Therapeutics. We like you, in your domains, want to leverage these modeling innovations to specifically better integrate precision neuromodulation with behavioral intervention for neural psychiatric problems like [inaudible 04:20:26] like CBT, like ERP, which I would argue is actually the change strategy that we need to be or enhance with our directive brain techniques. I'm keeping in mind this anecdote that Lena already shared about the freezing of gait in the lab. Maybe we want to be studying ticking phenomenon in Tourette. But we bring the patient into the lab, they don't tick for us. We're going to wire them all up. We're going to send them into their daily commute with their videos, and their sensors, and their microphones, and so on. I'm wondering for the panelists, how does centering on that patient's experience really highlight gaps or opportunities in model building? While I let you think about how you want to reply to that, I'll answer a little for myself, just highlighting again that in behavioral medicine, the patient is really the change agents. They are not a passive observer of events and responses like we are through the lens of data collection and model building. How do we approach model building such that the emerging technologies we develop from it really keep the patients in the driver seat? Not really an ethical question, it's more like a practical question, like how do we tap that force of an individual who's trying to make change in their lives? This question came to mind for me when Dani was speaking and boldly included the mind in her schematic. It also comes to mind for me when Scott is discussing, say, machine learning technologies to drive closed loop approaches. Or Maryam, what you've proposed in being able to simultaneously model behavior in brain. I'm wondering if that model them simultaneously. I'm wondering if that paradoxically actually gives us more freedom to involve the human in selecting the model inputs, including perhaps closed loop systems.

Dr. Maryam Shanechi: You mean the type of therapy, for example, or what do you exactly mean by input?

Dr. Allison Waters: Well, for you, what is the role of the individual's experience, their agency in how you think about and innovate your computational modeling approaches?

Dr. Maryam Shanechi: In close loop, we can definitely have some cooperative type system we design where we don't just let the machine dictate the optimal therapy parameters or dosage, for example. We allow the individual to also have a say in that, for example, the simplest version of this is an override. You can just override whatever this machine decides is best for your mental state. We can definitely think about a cooperative type system designs that allow some agency to the patient in terms of how they want to be treated. For example, maybe the machine can display what it thinks their mental state is, and on the basis of it just making a decision about the next level of simulation. Then on the patient if that's something they disagree with, maybe they can have an input there and whether we can put that within our actual computational framework to model this interaction between the human and the machine. That is also a very interesting problem to think about.

Dr. Allison Waters: Similarly, Dani, why did you choose to add mind to your schematic and not just make that a part of brain or behavior?

Dr. Dani Bassett: Because I think it's a really important. I think of behavior as something that does connect to the body with the environment and sometimes there are mental processes that don't necessarily come out and affect the environment, and so I wanted to have a place in the schematic diagram where the mind can be doing things that don't come out, but that could drive changes through the brain into the environment. I think that having that section is important. Those intentions or beliefs or goals or hopes or motivations, whatever it is. I think that we still don't have a part from a full understanding of how those mental processes are instantiated in the brain, and then from there, how behavior is altered. It feels like that section needs to be there because we don't understand it or its connection together with sub systems. I think that your idea or your example of the person who just doesn't tick in the lab, but does in their everyday life, I think it's fascinating and for me what that does is that it suggests that there is a dynamical regime that the person is working in their daily life and then when you change the environmental context in some way, they're in a different dynamical working regime, and that's the working regime of the lab. Then what the goal is, is to understand how do you move from one dynamical regime to another? How does a given pattern of interactions in each of these subsystems or between them, from behavior to environment, marine to environment, whatever it is, changes the landscape on what you're moving, and a lot of work has suggested that the pattern of interactions between these sub-components of each of the systems defines the nature of that landscape in some way. If we can unpack and understand that pattern of interactions more, it would provide us with a lot of intuition about how easy it is for the person to move from behavior to behavior, from cognitive process to cognitive process in a particular context or environment. That brings me back to the cognitive behavioral therapy, and I think you're right that it's an interesting challenge to combine that with other methods and understand how to use them together over different timescales or different frequencies to help the person enact change. You're raising a supercritical question and I think that these more complex approaches are needed to address it, but the particular way to do that still feels fuzzy in my mind.

Dr. Allison Waters: Gordon, you described behavior as essentially a filter between internal and external states.

Dr. Gordon Berman: I want to say that was my description, not what I think it is, but what most models treat it as. That was my criticism of most models.

Dr. Allison Waters: How do you feel like that metaphor is keeping things fuzzy, not clarifying?

Dr. Ming Zhan: Dr. Waters, you have one minute remaining.

Dr. Gordon Berman: I think in my mind, I'll try and be quick, is that it's basically in that it says the internal state is one thing. The internal state is really a set of things pushing and pulling against each other. From control theory, we know that a push-pull mechanisms, for example, are way more stable in a lot of cases than just having a single variable that we're trying to do a fix, like trying to have set control on. This notion of thinking about interactions between the states and how those states are then being fed back onto by the behavior, I think is almost a fundamentally different type of model. Then we're switching between different hidden Markov model type states. I think that is a fundamentally different way of viewing the world.

Dr. Allison Waters: Well, thanks for the brief conversation and I look forward to picking up these topics when I see you in person.

Dr. Ming Zhan: Thanks all. Thanks Dr. Waters for leading this great discussion. Then we move on to the second discussion led by Tayo Obatusin. Tayo, please take away.

Dr. Tayo Obatusin: Thank you for that. That was amazing set of talks and definitely learned a lot. My background is biomedical engineering, so I mostly focus on pragmatic application building development and essentially leveraging engineering principles to address the healthcare challenges and whatnot. In recent years, I've had the opportunity to work at the Center for Advanced Therapeutics working on treatment resistant depression. Previously at Emory and now at Sinai. In our center, and Dr. Waters has mentioned this in her introduction as well, essentially we are in the business of bio-marker identification for treatment resistant depression. Patients are fitted with a RC possess device where it allows us to collect brain recordings. Where on a daily basis state, they do recordings of their brain, recordings from wearables for activity and sleep, rating scales. It's very much in alignment with the theme of this workshop on brain and behavior quantification and synchronization. We're collecting a lot of data in the lab and even in a simulated environment where patients can essentially interact with a simulated environment and that allows us to capture as Scott had mentioned, R rhythms like open pose that that can be used to using transfer learning models and I wanted to riff on that because one of the things that strikes me is that we can develop really deep models for different sets of inputs, whether it's video, activity tracking, voice. But it's not quite clear how models can be developed for multi-modal data collection, and this is something that we're getting into as well where we can acquire multi-modal data along with including neural data. It's not quite clear how to build models that can integrate different multi-modal inputs. I was wondering if maybe Scott can speak to that and the rest of the panelists as well on how to better build these kind of models that integrate different multi-modal inputs.

Dr. Scott Linderman: Yeah, that's a great question. My camera sometimes does this weird zoom out thing. It's one that is not unique, I think, to the topics of this workshop in taking that bigger picture of where else in the broader ML world are we encountering similar analogous problems. There's lots of problems that have to do with modeling jointly images and captions, or speech and text, etc. These multi-modal modeling problems are ones that do come up quite often and I won't say that it's a solved problem, but there are ideas for how to do that and a lot of them start with positing some sort of a shared latent representation of both modalities at once and maybe trying to generate or explain as much shared variance between them as possible, while at the same time allowing for things that are unique to one domain versus the other. Maybe if you're measuring neural activity in some part of the brain, it may not have the necessary signals to predict certain aspects of behavior, and so you have to have some other way of explaining that otherwise unexplainable variance. These types of models are in some sense they're analogous or they appeared in Maryam's talk to some extent with shared latent variables predicting neural and behavioral measurements. Again, not to say that the problem is solved, but I think this is an active area of research both within our field and within the broader field as well. One that I'm optimistic about and that I think is an interesting area for research. While I have the mic though. I do also want to respond to a question that came up in the chat I think from David Anderson about encoding and decoding and asking, do we run the risk of inferring spurious non-causal relationships between neural activity and behavior analogous to a speedometer on an automobile where you can predict the position of the speedometer given measurement of the speed and vice versa. But if the car breaks down and all you know is about speedometers, you can't fix it. How can we go beyond these strictly correlational analyses to something that would give us more causal understanding? I think what this is getting at is that that sort of four buckets of organization is perhaps insufficient to explain all of the different types of challenges that we come up with, and if you had to add a fifth one, I don't know, I'm kind of torn here. I think that Gordon's emphasis on developing more a simple, theoretically grounded models is certainly one that's quite important, but an equally important one is establishing causal relationships between neural and behavioral data. We can start to do that without genetic tools, which I briefly mentioned. But is there a possibility for more causal inference from observational data? Certainly, this is an area that's an exciting area of ongoing research and it's one that I think we need as a field to have our eye on. Sorry Bill to steal a bit of your time there. But I wanted to make sure to get it out while I had the mic.

Dr. Ming Zhan: Yeah. We have one minute remaining.

Dr. Scott Linderman: I think what comes to mind, also like in the practical aspect of trying to use something like transfer learning, is sometimes I think about our data scientists I think who has tried to use something like decoding facial expression algorithm, which has been trained on six million videos around the world in measuring 16 different kinds of facial expression, some of these algorithms are not just easily obtainable, and you have to make a special request. The reason why this matters is because often before doing facial analysis, if you think about the constraints and the guidelines that are put in place for good reasons by IRB in some study design, you want to share individuals' videos out there. So you need to bring the algorithm home, so I think that's one of the things that I also feel that research community should be thinking about in terms of how to better leverage some of these big data tools that are available out there, but maybe not so easy to access.

Dr. Ming Zhan: All right, so we can conclude this discussion here. Thanks everyone, thanks Toluene to lead through this discussion. Now we move on to the third discussion, we want Dr. Tim Brown to lead the discussion.

Dr. Tim Brown: Hi everybody, I just want to say thanks to Dani Scott, Maryam, and Gordon for a series of very excellent talks. I also learned a lot. I might seem a little bit of a departure, I am a philosopher by training, and a bioethicist by profession. I'm here at the University of Washington School of Medicine in the Bioethics and Humanities Department. My biggest worries are about how we curate data, and the conclusions we reach through analysis of those data, and the impact of our conclusions on vulnerable groups downstream. I want to start us off by walking through a line of not so much argument, but more commentary, then I ask you a couple of questions that each of our panelists can answer. One thing that I've seen connecting all of the talks today, is that the idea that findable, accessible, interoperable, and reproducible data, fair data, will be vital to the creation of computational models from multimodal data. Having so many different sources of data, and synchronizing those data to produce insights that drive the models that we use in devices, in discovery and medical practice, it'll be extremely important to have these fair data practices to ensure that everybody has access to data. But we also need to reflect on fairness, accountability, transparency, and ethics of our data scientific practices. This is familiar from the AIML space where there's lot of institutional knowledge about how to make some headway on ensuring fairness, ensuring transparency and accountability. We need to mind these features of computational models of systems that data are recorded on, downstream uses of models and data. When research findings translate into devices, clinical practices, and ultimately lived experiences of patients. I think Dani is right. Behavior is a complex system, precisely because of the deep causal relationships between brains, behaviors, and the contexts that brains and behaviors happen. The statistical models that we apply to these data could be complex in ways that could be opaque, and that opacity could stand in the way of ensuring that our models drive systems in ways that lead to fair outcomes for users. We have to remember that metadata measurement and analysis can deeply impact how social groups are represented, not only in our models but in our medical scientific practices. For example, when much fomites groups are underrepresented in public datasets, or if data is subject to categorizations or characterizations, coming back to this question of how do we go from data to explanations of behavior that are blind to live of realities, our practices could create entire systems of misrepresentation of people's behaviors that are harmful to the groups downstream. To vulnerable groups downstream. One hypothetical later on, and this is my selfish worry, is the possibility of an adaptive DBS for depression that decode some neuro biomarker for depressive episodes is tuned using behavioral data like facial gestures, body language, that I'm assured is unbiased, but somehow overreacts to my emotional behaviors. Some moments, but is blind to me and others. But this is only one possible downstream moral consequence of these upstream decisions we make in the lab, how should data governance work, what role should vulnerable communities, thinking about indigenous populations, first nations, people who identify as LGBTQIA, what role should they play in the data curation practice? Now here is where I come to the questions. What is the most pressing ethical challenge each of you see arising from the curation of these complex multimodal data, and how these data drive the creation of complicated statistical models, and how do you see getting over these challenges? More specifically, how do we mitigate the risk of socialcultural harm in light of these challenges? I think in the order of the talks is great. I think I really want to hear from all of you, but maybe it will be good to start with Dani, and then move to Scott.

Dr. Dani Bassett: First of all, thank you so much for your comments. I think that raising these points is extremely important and glad that we get to end on them today. I think that the place where I see potential for harm and a lot of disparities right now, certainly is in the collection of data, but I think more where I focused is on how ideas are shared among scientists, and how ideas are valued across scientists. So it's more at this metalevel of whose ideas are being listened to, whose questions are being asked and reverberate through the system, and then help to guide the work moving forward. Some of them are quantitative work in my lab that's focused on those questions is related to citation patterns and how they are very skewed according to both gender, and race, and ethnicity, such that people who are from marginalized identities are under cited in comparison to what you would expect given the number of papers that they published, and the journals in which those are published and etc. Lots of factors that would soak up variance even after you account for all of those, there's still this very large gender and race and ethnicity effect. I think that that harms the science, because it harms scientists. It harms the people who are doing the work, and it alters who actually makes it to promotion and to receive a lot of the awards and etc. I think that I'm worried about that. I think that in terms of who we are collecting data from, that's a whole another question. Which is one I definitely care about but have less immediate expertise. So I'll pass it on to the next person.

Dr. Scott Linderman: Yeah, I completely agree. Thank you for raising these really important questions and points. I'll start by saying that I'm not an expert in AI fairness or anything of that sort, but I completely agree that this is a critical field for us to be pursuing. Actually, I would love to talk to you offline, sometime just to hear about your thoughts on that area of research.

Dr. Ming Zhan: Listen, we have one minute remaining.

Dr. Scott Linderman: I'll keep it short. Mostly has been on the basic science side. I just recently moved more in the translational areas, which has forced these issues to the fore. But even on the basic side, you see evidence of some of the things that you're concerned about there. Applying some generative models to mouse behavior. You find sometimes that the representations that you get for one mice versus another differ, not because they're fundamentally different in their behavior, but because one mouse is a little bit bigger than the other. Somehow in the feature extraction process, slightly bigger mouse ends up in a different part of the feature space, gets clustered, or modeled slightly differently. Now, we can go in and we can correct that and build in invariances one at a time, but it's done in a reactive way. I think one of the things that you're getting at is that as we deploy these systems in the real world in more translational settings, we absolutely need to be more proactive in getting out ahead of those types of biases before they adversely affect people.

Speaker 8: It's a great note to end on, I really hate cutting the discussion short, there went my timer. But I just want to give a shout out to everybody for such the hard work you have put into your presentations and keeping us on schedule and all the act of great discussions. We're going to close up today with some final thoughts from Karen Rommelfanger, and also from Justin Baker. So I will go ahead and hand the floor over to them and let them proceed.

Dr. Karen Rommelfanger: I understand that I have 10 minutes but I will use less, is that right, Dana?

Speaker 8: Yes. You have 10-15 minutes.

Dr. Karen Rommelfanger: Okay. Well, we're all tired, so I'll try to do 10, maybe even under. Thank you for sticking around for an incredibly rich and inspiring conversation. I was part of this discussion, not from the inception, but three years ago after the team had already given a lot of thought. It was just called BBQ and not BBQS, so the synchronization piece is an exciting new element. I'm charged with synthesizing new ideas, challenges, and some opportunities to address those challenges. I have three main points and then I have typically three bullets under those. By way of background, just for some of you who may not be aware, I haven't had the pleasure of meeting a lot of you yet, I'm trained as a neuroscientist and then moved into formal training in neuroethics and launched a neuroethics program at Emory and co-chair a neuroethics working group out of the International Brain Initiative, which is a consortium of the existing emerging Brain Initiatives at which brain is part of one of those. More recently, I moved into launching an independent international neuroethics think tank whose underwriting ethos is inclusivity across geographies and sectors. I feel like this is where we bring a very practical level to a lot of the ethics that we talk about and that we're going to need to think about in the next few days. The first point is that we have an ethical imperative for brain behavior quantification and synchronization, it's the type of activity I think that everyone here, and I think there were over 400 people online this morning, agree that brain should be taking up in some way. But in order to do that, we need tools and I think everybody here understands that the holy grail of neuroscience is still connecting the brain to behavior and we still have a lot of work to do in that space and maybe we'll have our whole careers to do that. I want to orient you to, at least at National Institutes of Health, there is a neuroethics working group of which I'm a part, and a neuroethics team. There, neuroethics is seen as a practical tool in your toolkit that can be used to scan the horizon, is not meant to set up roadblocks or to be purely a policing effort, which I think that RCR training has done to a lot of you in your perceptions of what RCR should be is what happened to me when I was in my training. But neuroethics can be used as a way to anticipate some of these ethical issues that Tim was bringing up and some others throughout the day and ultimately, can advance and accelerate science. With that in mind, we want to ensure that the work of NIH and science broadly is ethically advanced and also systematic in its exploration. I think Scott Linderman nicely mentioned them in the last piece. He said we want to get ahead, we want to be doing the ethics upfront. The second piece that I want to highlight is the challenge of describing what is normal when you start to quantify everything. Certainly, there are important reasons to want to quantify. A very powerful story I believe I've heard from some of the NIH folks is that psychiatrist and many of her patients who ended up committing suicide told her when she asked them that they would not commit suicide. Right now our tools for asking patients to subjectively report to us their internal state are course and falling short. How do we design studies and collect data where we can offer better explanatory power? How do we use non-human animals even to recapitulate these complex human conditions like autism? Being a team reminded us of an opportunity that diversity and variability. Consider those in your studies and actually that behaviors might be even more consistent than underlying neural activity. Jeffrey Cohn noted that a lot of these internal subjective states trying to draw that from our quantified data would be highly influential. We need to take care and we certainly need a bridge to think about the meaning of the behavior that we do mention. In thinking about quantifying, we need to remember that science isn't just about science and it never has been. Science is also intimately tied with power and it's important to consider who is driving parameters of normal and standardization. Jonathan Metzl, a professor of sociology and psychiatry at Vanderbilt, reminds us in his book that in unintended and often invisible ways, psychiatric definitions continue to police racial hierarchies, tensions and unspoken codes in addition to separating normal from abnormal behavior. Persons have become doubly or triply stigmatized based on unfounded generalizations about DBS, perceived volatility, abnormality or other characteristics that remain acceptable modes of discrimination. The rhetorics of health and illness become effective ways of policing the boundaries of civil society and keeping these people always outside. Even in our research phases, these are the types of things we need to get ahead of and that we need to be thinking about even as we design our research and our questions. Dorothy Roberts, scholar of race, gender, law, and civil rights at UPenn says that health cannot be divorced from its sociopolitical contexts and to do so would be to ignore the ways in which new biotechnology shape and are shaped by social power. Data privacy was brought up by Tim and will also likely be discussed heavily tomorrow. The implications for the inferences, even in research contexts, will likely end up still impacting areas beyond your laboratory and will likely interface, in your analyses, the publicly available data at some point. Kate Crawford, who Tim Brown mentioned in the chat earlier, leading scholar of social and political implications of AI, says that big data analytics will change how we know and likewise, we should expect more complicated ethical implications of what we know. Data is now infinitely connectable, indefinitely repurposable, continuously updateable and distanced from the context of selection. One of the toolkits that the NIH brain actually has some neuroethics principles. One of the principles says move beyond the bench with caution. Even as we consider the comparative work and the implications of our interpretation of the science, we should note that these technologies will not stay in the university and they likely shouldn't and they should likely move out into a number of domains and from the lab to clinic, consumer to national defense. I'm reminded that Paul Ekman's work was used to inform Immigration and Customs Enforcement. That's some of the work that we discussed today. The final point that I'll make is a suggestion for a framework which was asked for in the beginning by [inaudible 04:54:05]. It's a suggestion for a sociotechnical framework. This framework is thinking about our scientific and engineering challenges on equal footing with the social challenges and the social contexts and the implications of the work that we do in the lab. Dani [inaudible 04:54:20] noted that the mind is belief, desire, intention, and purpose and link that to the brain in a complex system. We should note that even that definition of brain is not culturally universal and that will have implications for how data is interpreted and how that research might end up feeding back into systems of health, including how different interpretations of how the mind and the brain are connected can have deep implications for stigma and application within medical systems and even beyond. Culture influences what kinds of science are supported and where science can be conducted and the types of ethical frameworks and evaluations of risks that happen. Gaps and understanding can lead to missed opportunities for collaboration and advancement towards future discoveries, limit the ability to broadly share results and thereby reap the benefits of findings and ultimately result in a failure to recognize the short and long-term potential and risk of neuroscience research. It's important to note that these cultural differences don't just exist amongst national entities, they exist within defined societies and also among individual researchers and practitioners. These are things that none of us are devoid of. Science doesn't happen in a cultural vacuum, science is actually contextualized. Another feature that I really liked that Dani [inaudible 04:55:40] mentioned, brain to behavior is not necessarily linear. It's not a simple causal chain. Any interpretation of the data that we find from any of the work that we might do in the BBQS framework needs to be similarly considered. What does it mean to put a brain in the context of the real world? Tim reminded us of many of the challenges that we'd have to explore. Importantly, ethics can advance neuro-technology and neuroscience and also ensure by thinking about ethics that scientists and the funders of it like NIH, NSF, social contract to society is met and sustained. The second part here is that we do need new tools and collaborations. Malcolm MacIver said that we need new tools for synthesis and new collaborators and then the chat there was a mention for just how many, maybe half a million authors is what we'd need to be able to tackle some of the most challenging neuroscience questions or more. But who should these collaborators be and who gets to decide who they are? Communities can be an important part of thinking of our collaborations with brain behavior quantification. There are opportunities for us to think about. We should consult communities and think about who might be impacted. We can consider communities as partners who might be able to give us even new insights into some of those tough questions we have about how far we can model autism in a non-human animal model and what kinds of conclusions we can draw and what kinds of utility we might find. Tim Brown raises questions about how to mitigate sociocultural harm with possibly vulnerable populations. Allison Waters mentioned a wonderful question. How does centering on the patient's experience and modeling highlight gaps for us to explore with BBQ? An interesting note is she said, this is not an ethical question, but it's a practical one. Actually, I would argue that it's both. These type of questions that are ethical questions can be very practically integrated into a science to help enhance and elevate that science. The second piece was Raji Baskaran and Peter Hartwell gave us great insights from industry. I think I'll never see a Chihuahua and a blueberry muffin the same way again. I don't know if anybody else felt that way. But Peter invited us to consider how to try new opportunities, how to think on a practical way to scale and translate in the real world beyond thinking about the types of challenges we might have as we stay in a headedness we have to our status quo of how we do science in an academic laboratory. The final thing that I'll say is there's this emphasis, this other thing like teen science. How do we do science? How do you create a value proposition of teen science? It's actually arguably just as much a social problem as a technical one. Dani, the set reminded us of the problem about who we sight even in our collaborations or as we think about the enterprise of science. We might also consider other out of the box partners in the chat way [inaudible 04:58:45] mentioned Arcadian of Science, and there's an existing movement happening probably almost entirely separate from this group called the centralized science, which is also exploring active tools on how to democratize the scientific process and hope in science practices. That's my summary for today where there's a lot of rich discussion and a lot of opportunity. I hope this put out a few seeds for some conversation for tomorrow's breakout groups. I'm honored to be here with all of you and to be thinking through this with you today and tomorrow. Thank you.

Dr. Justin Baker: I think I can go last then and I'm not able to turn my video on. I'm just going to share my screen for one second as I go through some of my impressions from the day. I think we're all reeling from just the extent of the depths of what we've discussed today. But I'm Justin Baker, I'm Assistant Professor of Psychiatry here at the Medical School and Scientific Director for something called the Institute for Technology and Psychiatry here at McLean Hospital. I think some of the themes that resonated to me really applied to some of our own work, which is thinking about how do we assess mental health going beyond the typical case-control models that we've had to wrestle with in the past, given the complexity of co-morbidities. Also obviously, as we've talked about today, just the complexity of looking at variation that we see at the level of patients or organisms and trying to make sense of the causal chain of events that goes to all the way down to genetics and all of the other intermediate skills. On top of this, which by the way, is usually something we infer as a field across many thousands of individuals, we usually don't do it at the level of individuals. Yet with humans, as well as other organisms, we have to think about mental health evolving over the lifespan, as well as over periods of days to months to weeks as individuals change their [inaudible 05:01:05] state. These just add to the complexity of what we're trying to solve for and trying to understand the brain spaces for behavior. One of the issues we've tried to wrestle with, when you heard from Jeff Cohn earlier, sessions about dyadic encounters being the main way that clinicians and often clinical researchers evaluate mental health, it's just not a very good system to come up with strong point estimates for an individual's mental state. Like Jeff Cohn's group, we've been working on other methods to capture those information from video data. But ultimately, the way we assess mental health today is mostly open loop, and we talked today about various closed-loop waves we can begin to assess mental health. I just wanted to come back to this notion of a control system which we've heard about today in several of the sessions. Which is that as we try to understand any system where there's a latent construct, we're going to have some sensor networks providing raw information. Critically, it's not just the raw signals that we need to pay attention to. It's relevant features that get extracted from those raw signals. We heard a lot today also about the idea that behaviors in many cases are there to help reorient our sensors and get additional information. Not the only reason we have behaviors, Ben Hayden and others mentioned that behaviorists are also necessary for survival. But it's very important that we think about our sensory systems and motor systems as acting within these closed-looped environments. What I like to point out both to a technical audience as well as to engineering audience is fundamentally the brain is a bunch of these closed-loop systems trying to compute information about the world to solve those survival problems. It's very much relevant to the way neuroscientists might think about the world. But it's also quite relevant to how clinicians think about the world. Every time a clinician needs to interview a patient, they have to use their own sensory information they've honed or evolved through training to extract relevant information from their patients. But it's really not used in a really systematic way. But the same concept is fair that clinicians are constantly doing this and iterating towards solutions that are parsimonious with all the evidence. In our own work, we tried to use that same approach to put actual sensors on patients and to combine those much higher density type assessments like video with the lower density assessments like wearables, to try to see whether signals of clinical relevance are present in each of those different sources of data. Just to make this more concrete, we think of many different raw data that we can pull from in today's environments, from self-reports and surveys all the way through to electronic health records and then increasingly all these other types of data that we heard from several of the presenters on today. We heard, again ways to get it from computer vision. We didn't hear as much about MRI, but ultimately we can try to combine all of the relevant features from raw signals. But ultimately it's about informing the latent constructs that are relevant for patients if we're trying to work on clinical applications. To take it even further out, we think of this as where mental health assessment will go, which is that we'll have these systems of comprehensive phenotyping that try to link together different data sources. But ultimately try to do that through relevant latent constructs that we know aren't going to have the exact same mapping in every single patient that we encounter. But that by understanding where those mappings are more reliable, we can begin to have better systems that are able to work well, both at the individual level and applied to groups. I won't go into any of this today, but I think we've heard a little bit about ways that we can begin designing consumer experiences to actually leverage changes in these signals to provide better care systems, and also be able to anticipate changes in care capacity and things like that that are relevant for care organizations. I just wanted to briefly mention a study that we've been doing with support from the NIMH, it's part of what's called the intensive longitudinal health behavior network. It was an experiment that Danish philosopher, one of the organizations today was very much involved with that actually spanned multiple of the NIH institutes from National Cancer Institute as well as AAA, to really try to use these multi-modal, multi-level assessments to follow individuals with a whole range of different health conditions or for longer periods of time that we can begin seeing common elements from their pathology as well as things that are specific to the condition being studied. What our group has been focused on is following 100 individuals for at least one year who are likely to experience depression, bipolar disorder, or a psychotic condition, and then we try to put into register all of their self-report as well as clinical evaluations and other objective measures. I think just to highlight that these are the data that we can begin to collect at scale where we can hit something which, you can think of it as a single pixel camera or three pixel camera on the wrist wearable, where periodic encounters of a video. To try to find individuals who are going through significant change in their clinical status to try to understand how these signals are changing in meaningful ways. Again, just to highlight that the concept of this network was to encourage projects to not just focus the construct that they were most interested in, but also to focus in on all behaviors that might be common across the humans in the study. I think just from hearing the talks today, the different sessions, we can begin to think about ways to motivate similar studies that are across species nature where even if you're not necessarily interested in grooming behavior, you would nonetheless collect enough high density data of other adjacent behaviors around your contrast of interest to be able to inform a more data-driven assessment in line with other studies collecting similarly granular data. I'll just show you one quick example of the data that we can get from a single participant, so this is someone that we followed for over two years. As you heard from some of the other talks today, we can ask them questions on a smartphone, questions that are loosely grouped into positive and negative feelings, and see that this individual experience really profound long periods of positive effect, followed by profound periods of negative effect, and then again, positive effect. You can see that there's a fairly dense periods, even though the periods where she's experiencing positive and negative effect change, nonetheless, they're quite dense. Then I think as we would start to see this, it's not exactly ground truth, but it's a very strong indication of what stage she is in. We can then add other clinical measures such as the very low density assessments that we would do from clinical assessments every month to show how they are more or less correlated with the self-report, but obviously delayed and much less temporally dense. Then we can combine those with other very dense assessments from a wearable. Today I don't want to get into too much of the science here, but just to point out that we do start to see really striking changes, as was brought up in one of the early comments about when someone does change from depression to not being depressed, what's the sequence? Do they first feel better and then they look better? Here we see very striking changes in those individuals. Sleep pattern, both the pattern of how they're sleeping, but also the level of activity during the day, which roughly speaking does change in accordance with those other subjective states. We already see that in these examples like this, by following people over long periods of time, we began to capture that naturally occurring phenomenology that we studied in the laboratory, usually only in a single time point. I think it's just as we would with other complex systems that we only really have ability to study the latent constructs. Nonetheless, we can follow an individual or groups of individuals over a long enough period of time where we can begin to actually resolve some of these relationships and begin to have much stronger hypotheses for what causal systems are underlying. I won't deliver it today, but we have developed a whole energy allostasis, homeostasis model based on this that we think is very much testable in larger populations. I'll just end my comments by saying that a lot of this work I think is really geared towards moving beyond caricature views of what mental illness is or what some of the underlying behaviors would be to really situate those observations in real-world situations, and to be able to connect subjective experiences with things that are objectively measurable. I think we're certainly doing this and try to help build the tools to do this, to be able to collect much larger datasets than just 100 that we're discussing here, but we used to take those same ideas and then scale them up into the thousands of individuals. I will also just end by noting or sometimes ask whether eventually a psychiatry is just going to be replaced by artificial intelligences. As part of a debate with the British Journal of Psychiatry a couple of years ago where I was coming down against this notion. But I do think it's worth thinking about what are the tools that are going to eventually replace what a human in the loop is doing, and what are the roles that are going to continue to be performed by humans? I think of relevance to some of the other ethical considerations we talked about today, which is, how do we know that a particular set of tools is actually ready for a particular use and who gets to decide? Is simply a question of the marketplace. What people are willing to spend their money on. Is it the government regulations that determine this? Or is it simply that the physicians who have to deal with these very complex, challenging issues every day they're going to start to turn to whatever solutions are out there, even whether the evidence is strong or not. Also, just to mention that Timothy Brown's question in the last session. We also take the ethics of this work very seriously because I think there is this question of whether we can move beyond the bench with caution, but I think it's also the case that many of these analytical techniques and technologies are now available, and so I think the patients who ultimately are experiencing this conditions really deserve application as soon as it's possible. As soon as it's not going to be unsafe for them to do so. As part of our work, we were trying to move as aggressively towards patient applications as possible, and so we recently published an ethics checklist for digital health in this area given many of the complexities around how you achieve informed consent with participants in these multi-modal very longitudinal studies, as well as ensure equity, diversity, and access, privacy, regulations, and importantly return of results. With that, I will wrap up my comments and again, just want to thank folks for inviting me to participate and all of the amazing speakers that we had today. Appreciate it.

Speaker 5: Thank you so much, Justin. Thank you Karen. I really appreciate that both of you ending us on this talk. I would like to also note that I know that the discussion time seemed very compact, the talks were very short, high-level conceptual talks. I hope this wets your appetite for the discussions that all of you participants are going to be taking part of tomorrow. Tomorrow will be the three more high-level talks and then will be followed by two concurrent breakout sessions where we'll get to dig into more of these thoughts and ideas that were brought up, and then we'll follow up with a summary and conclusion. With that, I will close the meeting and thank you everyone for sticking it out for this long night.