**Intro to Neuroscience, Seminar, CalTech Mice Social Interaction**

**Related articles and their main takeaways**

**Wiltschko, A. B., Tsukahara, T., Zeine, A., Anyoha, R., Gillis, W. F., Markowitz, J. E., ... & Datta, S. R. (2020). Revealing the structure of pharmacobehavioral space through motion sequencing. *Nature neuroscience*, 23(11), 1433-1443.**

The article showcases the success of the MoSeq method in finding similarities and differences in a mice behaviour when they are administered different drugs. To cite the abstract:

“MoSeq identifies syllables that are characteristic of individual drugs, a finding we leverage to reveal specific on- and off-target effects of both established and candidate therapeutics in a mouse model of autism spectrum disorder. These results demonstrate that MoSeq can meaningfully organize large-scale behavioural data, illustrate the power of a fundamentally modular description of behavior and suggest that **behavioural syllables represent a new class of druggable target.”**

For our project, it matters for three main reasons:

1. **Deep learning method as a viable and promising tool.** MoSeq (3d imaging + unsupervised machine learning) is shown to be successful in identifying and distinguishing the different behaviour structures and characterising altereation resulting from experimental interventions.
2. **Applications:** pharmacology and use of MoSeq and similar tools for new drug testing. Behavioural syllables as a new therapeutic target. “Fingerprint” of a drug
3. **Potential direction for model:** identifying “syllables” – behavioural motifs such as head-bob or tail-turn underlying behaviour that is labelled “angry” or something else. I think we do not have enough data for this, but idea is cool.

Shows limitations of our data and what is possible when more variables are available. Third dimensions more precise results, and allows for better syllable identification, which is not surprising but good to mention in notebook, cause what we have is a scalar summary.

Other:

* Phenotypes are encapsulated by small subsets “LASSO regression analysis revealed that most of the information required to tell individual drugs apart from each other resides in a small subset of syllables” p. 1493
* “Our **proof-of-concept experiments** provisionally linking the differential expression of particular syllables to the modulation of specific receptors (made possible by phenotyping different drugs with distinct but overlapping receptor specificities) suggest that this sort of mapping could also enable accurate predictions of the mechanism of action of a drug from behaviour alone.” P. 1441
* Examples of deep learning-based platforms for behavioural sequencing include LEAP, DeepLabCut and DeepPoseKit
* Has good additional info on modelling and statistical methods used, could be helpful?

**Cepelewicz, J. (2019, December 10). *To Decode the Brain, Scientists Automate the Study of Behavior*. Quanta Magazine.** [**https://www.quantamagazine.org/to-decode-the-brain-scientists-automate-the-study-of-behavior-20191210/**](https://www.quantamagazine.org/to-decode-the-brain-scientists-automate-the-study-of-behavior-20191210/)

Popular science article which nicely introduces the changes in behavioural studies and how is Machine Learning is changing that game.

* One of the big question is “How do we define the building blocks of behavior, and how do we interpret them?”. Traditional ethology (study of animal behaviour) studies would rely on extensive observations accompanied by the most detailed description possible to be noted by the scientist’s eye. Not surprisingly, ML is way more accurate.
* They’re using these automatic classifications to discern the behavioural effects of different gene mutations and medical treatments and to characterize social interactions.
* “We know that this grammar is directly regulated by the brain. It’s not just an epiphenomenon, it’s an actual thing the brain controls.” Datta
* The idea of automatic classification is to discern behavioural effects resulting from medical treatments and gene mutations, as well as characterizing social interactions. The simple idea for us could be maybe just to build a model that discerns aggressive vs non-aggressive behaviour and see how it correlates with the actual labels. But it is not enough data again, or is it?
* Behavioral grammar is NOT epiphenomenon, it is directly controlled by the brain.
* Examples of what has been done: “. They had previously created a model that used measurements of the flies’ movements to predict when, how and what the male fly would sing. They discovered, for example, that as the distance between the male and female flies decreased, the male was likelier to produce a particular type of song.”

***AIcrowd | Multi-Agent Behavior: Representation, Modeling, Measurement, and Applications | Challenges*. (n.d.). AIcrowd | Multi-Agent Behavior: Representation, Modeling, Measurement, and Applications | Challenges. Retrieved 2 November 2023, from** [**https://www.aicrowd.com/challenges/multi-agent-behavior-representation-modeling-measurement-and-applications**](https://www.aicrowd.com/challenges/multi-agent-behavior-representation-modeling-measurement-and-applications)

The initial challenge for which the dataset was meant for, just in case someone did not see.

**Problem:** The "annotation bottleneck", where manual annotations get in a way, as it can be too slow or individual annotators might converge on their interpretations of behaviour

Partial solution: pose estimation software

The remaining challenge is to **close the gap between tracking and behavior**: given just the output of an automated tracker, can we detect what actions animals are performing? Moreover, can we learn different annotation styles, or to detect different behaviors, without having hours of training data to rely on?

Originally three tasks:

1. Classification
2. Annotation Style Transfer
3. Learning New Behavior

**Datta Lab, one of the main ones in the field of neurobiology, animals and their brainshttp://datta.hms.harvard.edu/research/overview/ (not for citing)**

Assumption: **evolutionary inherited sequences, thus at least partially predictive. The question is to what extent?**

“Animals engage with the world through **structured movement**: think of a hungry mouse rustling through leaves on a forest floor to find food, or of a peacock rattling its train to attract a mate. These natural behaviors — often pre-specified by evolution, but also flexibly adapted based upon context and experience — are built by the brain out of simpler behavioral elements that are placed into **meaningful, fluid sequences.”**

But

* Not only goal-oriented behavior
* “Instead, much of what most animals spend their time doing is exploring — using movement and their senses to better understand the world around them.”
* The problem: how do we interpret that?

**Datta, S. R., Anderson, D. J., Branson, K., Perona, P., & Leifer, A. (2019). Computational neuroethology: a call to action. *Neuron,* 104(1), 11-24.**

Article draws on the main opportunities and challenges that are presented in neuroethology—the science of quantifying naturalistic behaviours for understanding the brain. In other words, leveraging naturalistic behavior to explore brain function.

Figure 1 Challenges in Computational Ethology

Paveikslėlis, kuriame yra tekstas, ekrano kopija, Šriftas

Automatiškai sugeneruotas aprašymas

* Bringing psychology, neurobiology, and ethology together to a more integrated study
* Lots of good work so far “Studying neural activity as animals behave freely has led to some of the most exciting discoveries in brain science over the past 50 years, including place cells (Hartley et al., 2013), grid cells (Rowland et al., 2016), replay (Foster, 2017), mechanisms of nonassociative learning (Kandel et al., 2014), and the escape response (Medan and Preuss, 2014).” (p. 13). Usefulness
* But so far focus on a simple behavior that is easy to quantify without restraint.
* Alternatives for “syllable”: ‘‘motifs,’’ ‘‘modules,’’ ‘‘primitives,’’ and ‘‘movemes’’
* Naturalistic behaviour and neural activity similarities: high dimensionality, time-evolving structure, variability, and organization at multiple temporal and spatial scales (Panzeri et al., 2015)

Paveikslėlis, kuriame yra tekstas, ekrano kopija, Šriftas, dizainas

Automatiškai sugeneruotas aprašymas

Three main things to consider when measuring behavior:

1. **Timescale**: if possible, organize labels hierarchically, to not undermine the multi-scale aspect of behaviour
2. **Interpretability:** descriptions leading to hypothesis generation
3. **Prediction:** standard for quality of behaviour representations (neural in comparison to behaviour)

**Wiltschko, A. B., Johnson, M. J., Iurilli, G., Peterson, R. E., Katon, J. M., Pashkovski, S. L., ... & Datta, S. R. (2015). Mapping sub-second structure in mouse behavior. *Neuron*, *88*(6), 1121-1135.**

“Main Highlights:

* Computational modeling reveals structure in mouse behavior without observer bias
* Mouse behavior appears to be composed of stereotyped, sub-second modules
* From this perspective, new behaviors result from altering both modules and transitions
* Unsupervised analysis reveals how genes and neural activity impact behavior”

This showcases that models proves that people are not just reading into it, mouse body language does have what has been called “syllables” and “grammar” (alternative names including: motor primitives, behavioral motifs, motor synergies, prototypes, and movemes, syllables as the chosen due to analogy to birdsongs).

* “The behavioral modules identified by the AR-HMM here find their origin in switching dynamics that are expressed on timescales of hundreds to milliseconds” so not our dataset
* Modules/syllables do not exist in isolation, but are given meaning trough the transition sequence, and these statistical interconnections become “grammar”