Tracking information flow throughout the mouse brain using regional population decoding in a forced choice task

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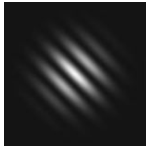
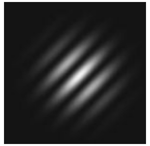
Plan

- Background
    - Steinmetz et al. (2018) reported neuron populations, globally distributed across the brain, which where non-selectively activated in the time, leading up to movement-onset of mice
- Scientific question
    - How is information integrated across involved brain areas? How does integration give rise to motor behavior?
- Planned analyses
    - Population decoding, classification of motor-behavior, cross-validation of results.

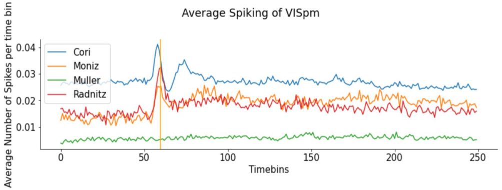
Information Flow

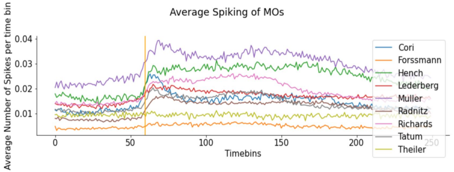
Stimulus

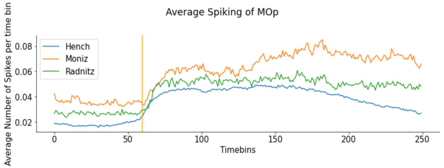




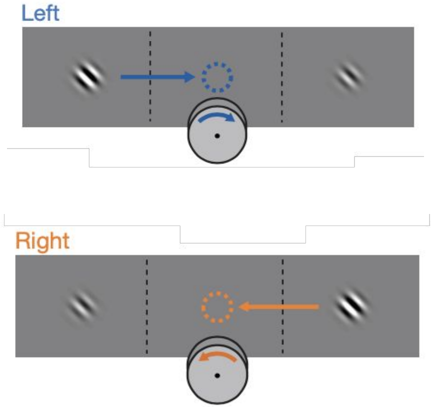
Neuronal Response



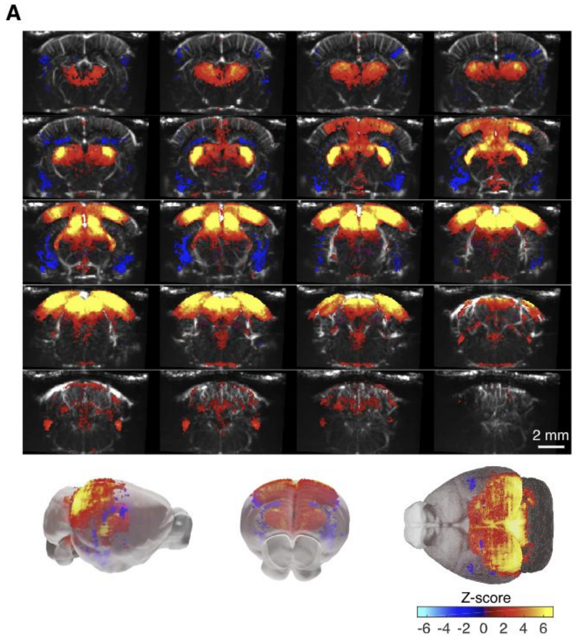




Behavioural Response



Scientific Question



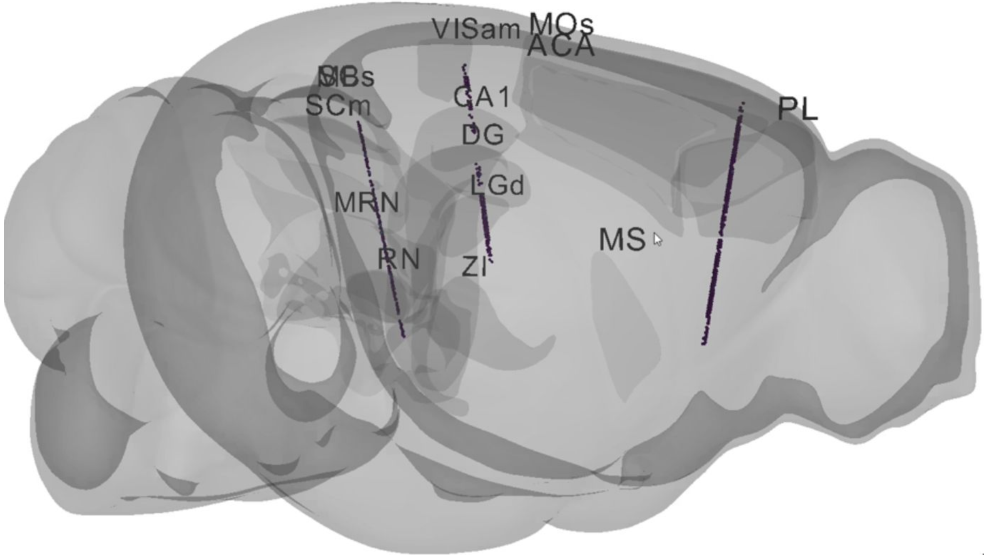
Mace, E., et al. (2018). Whole-Brain Functional Ultrasound Imaging Reveals Brain Modules for Visuomotor Integration. *Neuron.*

- What areas can be identified by a decoding model as being involved in processing the visual stimuli and planning motor response?
- How accurately can specific regions predict a motor action from the Steinmetz dataset?
- What is the information flow from visual stream to motor processing and are region specific populations better predictors of behavioural outcomes?

Are there regions that can predict correct and incorrect trials?

Dataset

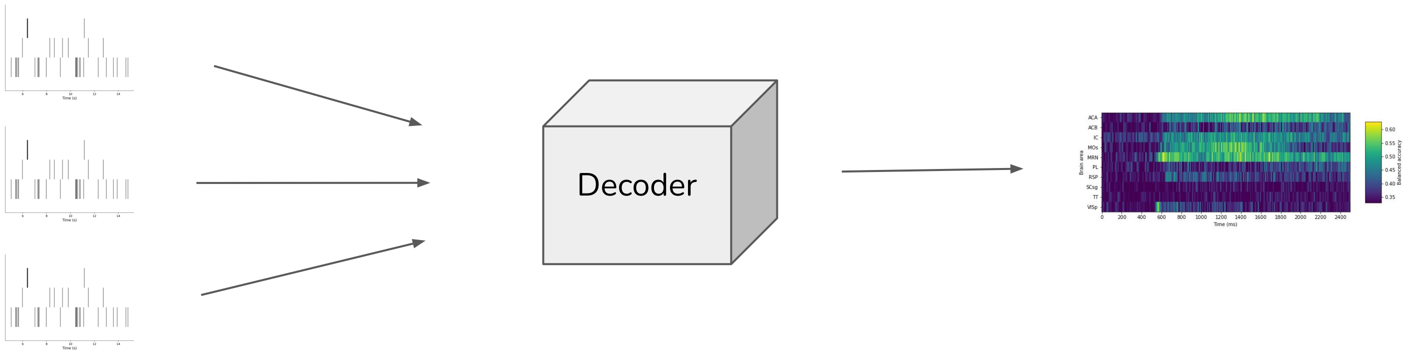
- 39 recording sessions from 10 different mice
- Preselection of good neurons obtained via spikesorting
- Neurons are assigned to brain regions (different regions in each session, 73 regions total)
- Spike counts in 250 timebins (10ms) from 500ms before stimulus onset to 2000ms after



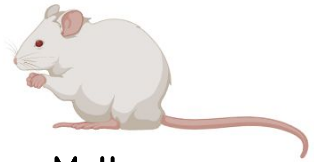
Exemplary anatomical location of probes/channels in Allen Mouse Brain Atlas (mouse Lederberg)

Methods

- One model per timebin and per brain region
- **Decoding motor behaviour:** predict motor actions (left/right/nogo) from spike counts using l2-regularized logistic regression (one-vs-rest)
- **Decoding visual stimulus:** predict delta-contrast (i.e., difference between left and right stimulus) from spike counts using ridge regression
- **Decoding error trials:** binary classification (correct/incorrect trial) from spike counts using l2-regularized logistic regression
- All analyses use 5-fold cross-validation



Regional Classifiers



Muller

Predicting visual stimulus contrast

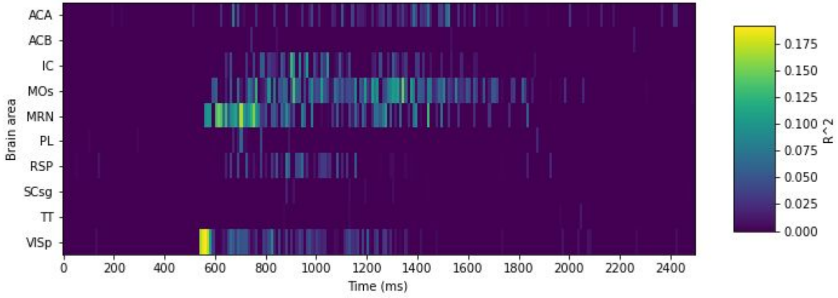


Figure 1. Coefficient of determination of ridge regression from neural activity to visual stimulus (contrast left minus contrast right) over time for different brain areas. Data corresponds to one representative animal (Session 21).

Predicting motor-action from correct trials

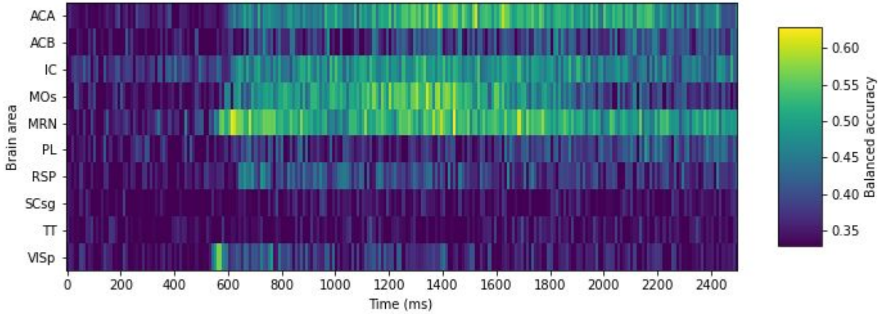
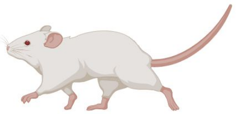
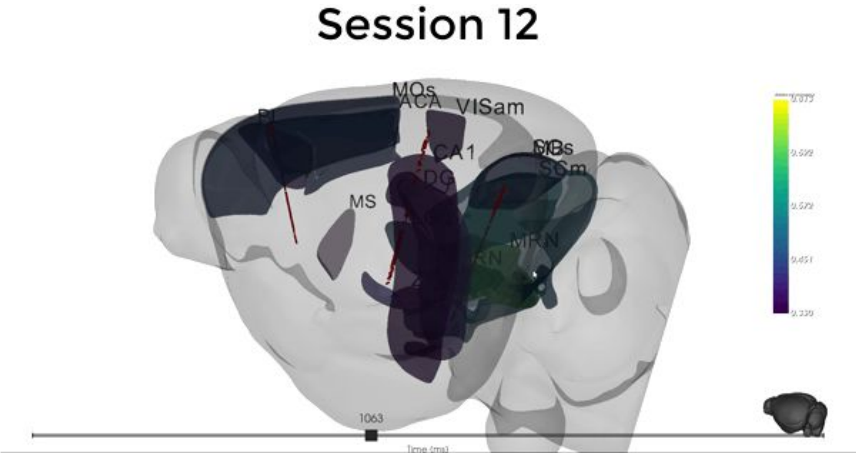


Figure 2. Classification accuracy of l2-regularized logistic regression over time for different brain areas. Class labels are motor-outcome (left/right/no-go; only trials with correct movements). Chance level is 33%. Data corresponds to one representative animal (Session 21).

Results - Prediction of Motor Action



Lederberg



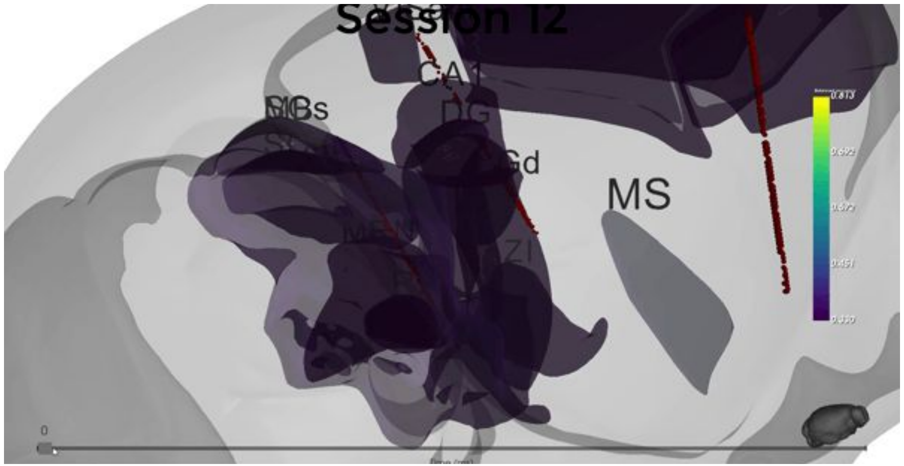
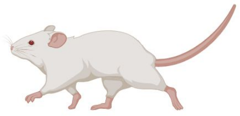


Figure 3. Brain render of active areas recorded in session 12. Color coding shows the prediction accuracy of the model for identified brain regions (ACA, CA1, DG, LGd, MB, MOs, MRN, MS, PL, RN, SCm, SCs).

Figure 4. Brain render of active areas recorded in session 12 depicting the region specific classification accuracy over time (from 0.5s before to 2s after stimulus onset).

Results - Decoder Weights



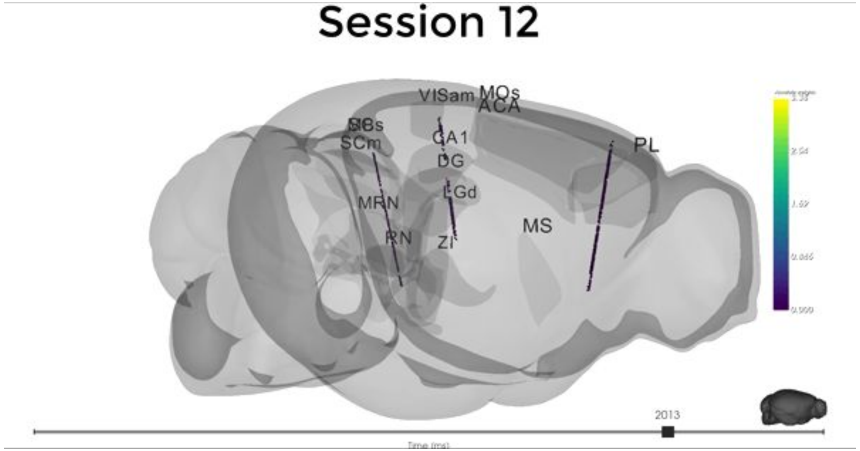


Figure 5. Anatomical position of probes in Session 12.

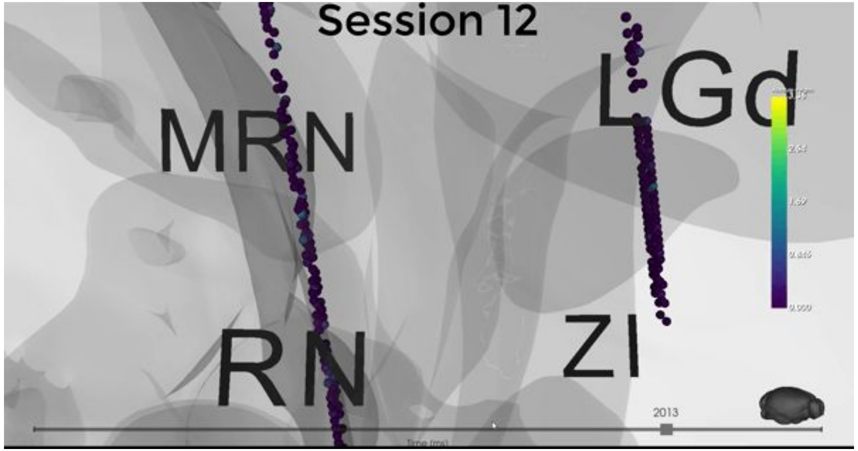
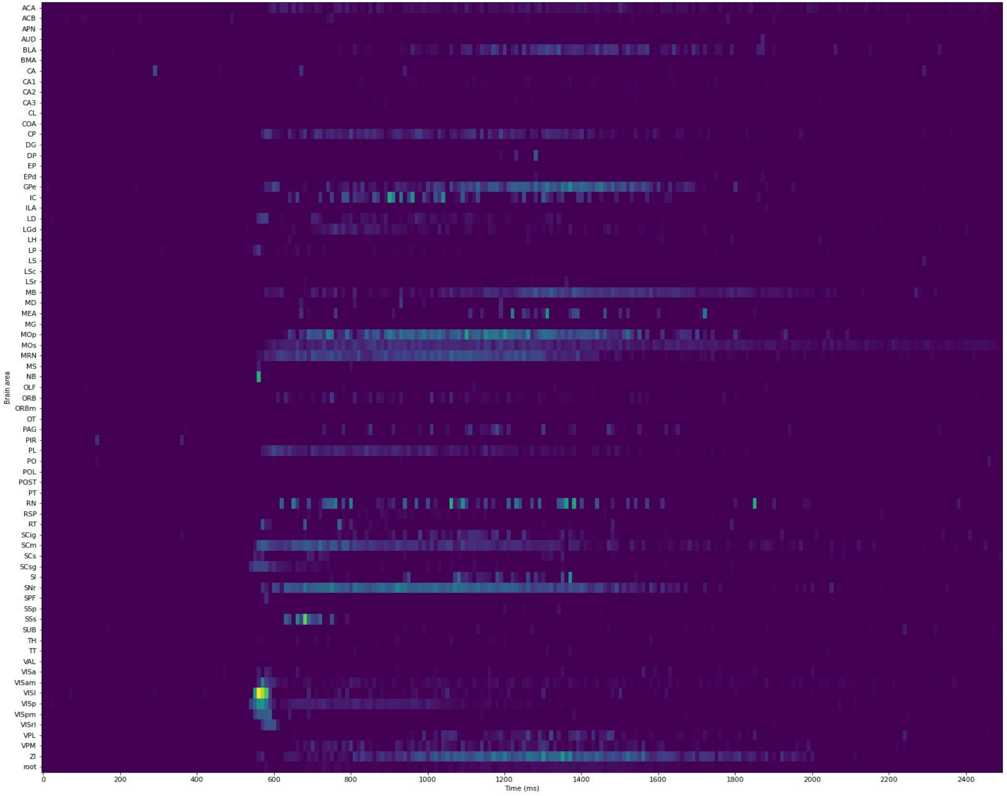
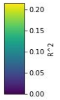


Figure 6. Classification weights from the decoder trained on the full whole brain decoder**.** Depiction of classification weights, as gained from decoded on whole brain data.

Result - Visual stimulus decoding



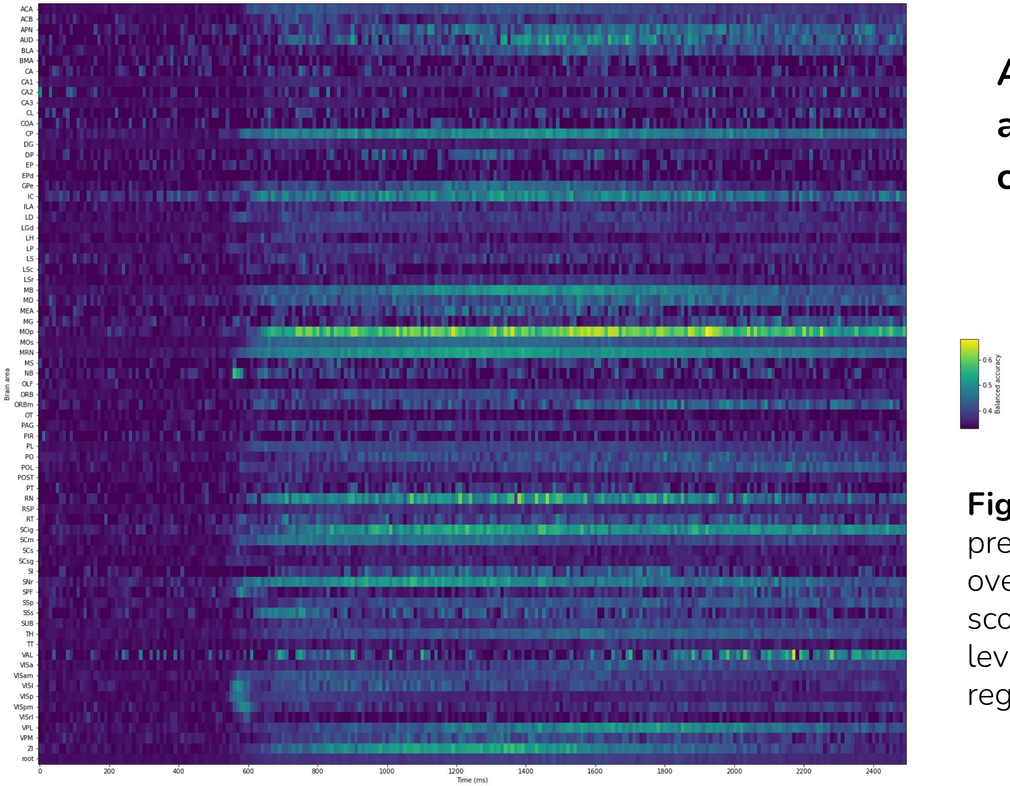


Above-chance classification accuracy for stimulus contrast

- Visual areas (Lateral visual area, primary visual area)
- Motor areas (Primary motor area, secondary motor area)

Figure 7. Coefficient of determination of ridge regression from neural activity to visual stimulus (contrast left minus contrast right) over time for different brain areas. Data corresponds to average per brain area across mice and sessions.

Result - Decoding Motor Behaviour

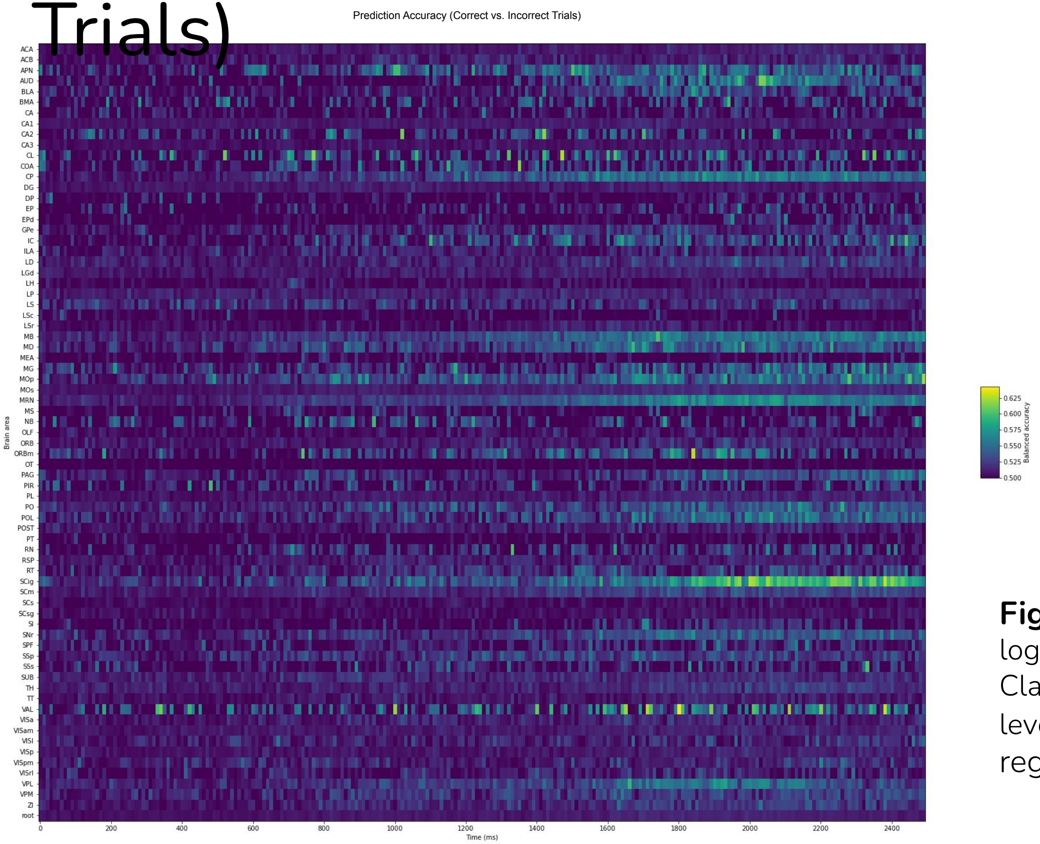


Above-chance classification accuracy for motor behavior from correct trials

- Primarily motor areas (Primary motor area, secondary motor area, MRN)

Figure 8. Contribution of different brain areas in predicting motor behaviour (left, right, nogo) over time. Values indicate balanced accuracy scores of a logistic regression model. Chance level is 33%. Scores are averaged per brain region across all mice and sessions.

Result - Predicting Errors (Correct vs Incorrect Trials)



Above-chance classification accuracy for motor-outcome

- Motor related areas (Caudoputamen, Superior Colliculus, Primary Motor)
- Non-visuomotor areas also returned high prediction accuracy (MGN and MD)

Figure 9. Classification accuracy of l2-regularized logistic regression over time for different brain areas. Class labels are trial-outcome (correct/incorrect). Chance level is 50%. Data corresponds to average per brain region across all mice and sessions.

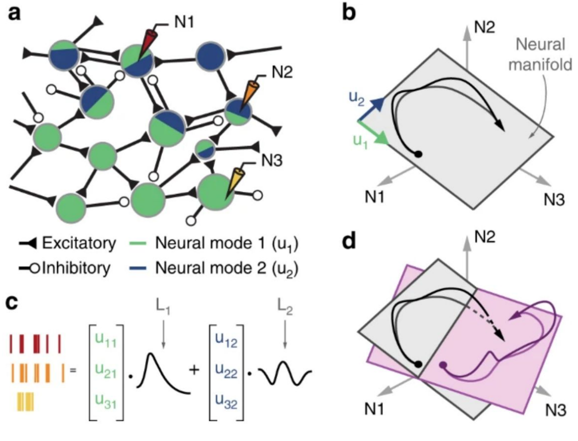
Limitations

- Motor execution and stimulus are highly correlated.
- Averaging over mice, across sessions.
- Placement of probes.

Abbreviation	Full name	N recordings	N mice	N responsive neurons	N total neurons	% responsive
ACA	Anterior cingulate area	11	8	395	608	65.0
ACB	ACB Nucleus accumbens	3	3	152	255	59.6
APN	APN Anterior pretectal nucleus	2	2	177	235	75.3
BLA	Basolateral amygdalar nucleus	2	2	107	261	41.0
CA1	Field CA1	21	10	494	1129	43.8
CA3	Field CA3	10	6	243	438	55.5
CP	Caudoputamen	5	5	524	914	57.3
DG	Dentate gyrus	16	10	336	711	47.3
GPe	Globus pallidus external segment	3	3	146	274	53.3
ILA	Infralimbic area	3	3	192	338	56.8
LD	Lateral dorsal nucleus of the thalamus	6	5	209	308	67.9
LGd	Dorsal part of the lateral geniculate complex	10	5	397	811	49.0
LP	Lateral posterior nucleus of the thalamus	11	8	393	732	53.7
LS	Lateral septal nucleus	7	5	508	844	60.2
MD	Mediodorsal nucleus of the thalamus	3	3	244	381	64.0
MG	Medial geniculate complex of the thalamus	2	2	180	276	65.2
MOp	Primary motor area	3	3	553	682	81.1
MOs	Secondary motor area	19	9	993	1534	64.7
MRN	Midbrain reticular nucleus	11	7	722	857	84.2
OLF	Olfactory areas	9	5	210	684	30.7
ORB	Orbital area	6	5	281	770	36.5
PAG	Periaqueductal gray	3	3	72	130	55.4
PL	Prelimbic area	10	7	438	728	60.2
PO	Posterior complex of the thalamus	5	4	342	620	55.2
POL	Posterior limiting nucleus of the thalamus	3	3	132	190	69.5
POST	Postsubiculum	4	3	163	272	59.9
RSP	Retrosplenial area	9	5	308	598	51.5
RT	Reticular nucleus of the thalamus	2	2	111	160	69.4
SCm	Superior colliculus motor related	11	6	738	997	74.0
SCs	Superior colliculus sensory related	10	6	192	317	60.6
SNr	Substantia nigra reticular part	4	3	201	274	73.4
SSp	Primary somatosensory area	5	4	296	461	64.2
SUB	Subiculum	9	7	494	669	73.8
VISa	Anterior visual area	5	4	207	285	72.6
VISam	Anteromedial visual area	11	8	501	805	62.2
VISl	Lateral visual area	3	2	248	403	61.5
VISp	Primary visual area	12	8	649	923	70.3
VISpm	Posteromedial visual area	4	4	230	516	44.6
VISrl	Rostrolateral visual area	2	2	85	236	36.0
VPL	Ventral posterolateral nucleus of the thalamus	4	3	202	255	79.2
VPM	Ventral posteromedial nucleus of the thalamus	4	2	235	357	65.8
ZI	Zona incerta	4	2	167	220	75.9

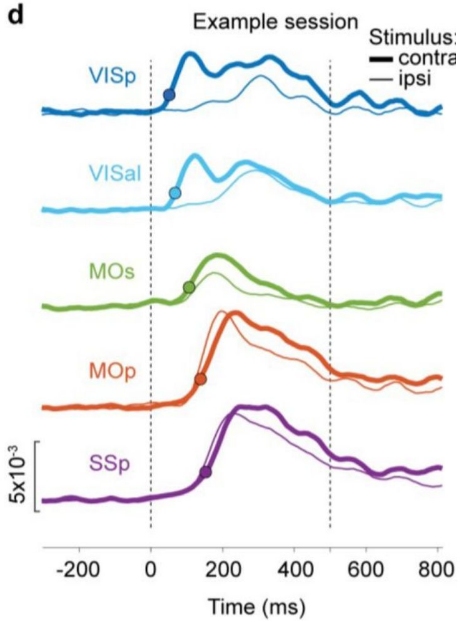
Learnings - Initial Expectations

Manifolds



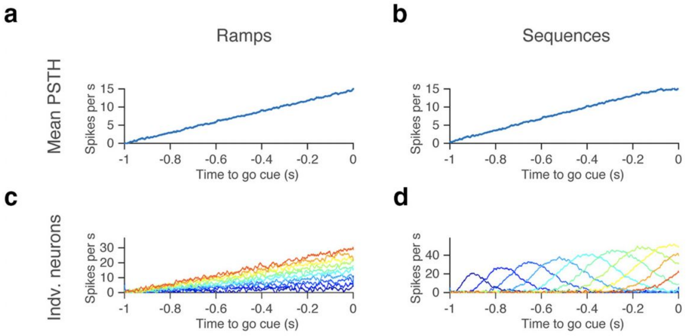
Gallego, J.A., et al (2017) Cortical population activity within a preserved neural manifold underlies multiple motor behaviors. *Nature Comms.*

Clear "flow"



Bulkin, D. A., & Groh, J. M. (2012). *Distribution of visual and saccade related information in the monkey inferior colliculus. Frontiers in Neural Circuits, 6.*

Early prediction via Ramping



Li, N., Daie, K., Svoboda, K., & Druckmann, S. (2016). *Robust neuronal dynamics in premotor cortex during motor planning. Nature, 532(7600).*

Thanks

- Team Slick Mice -

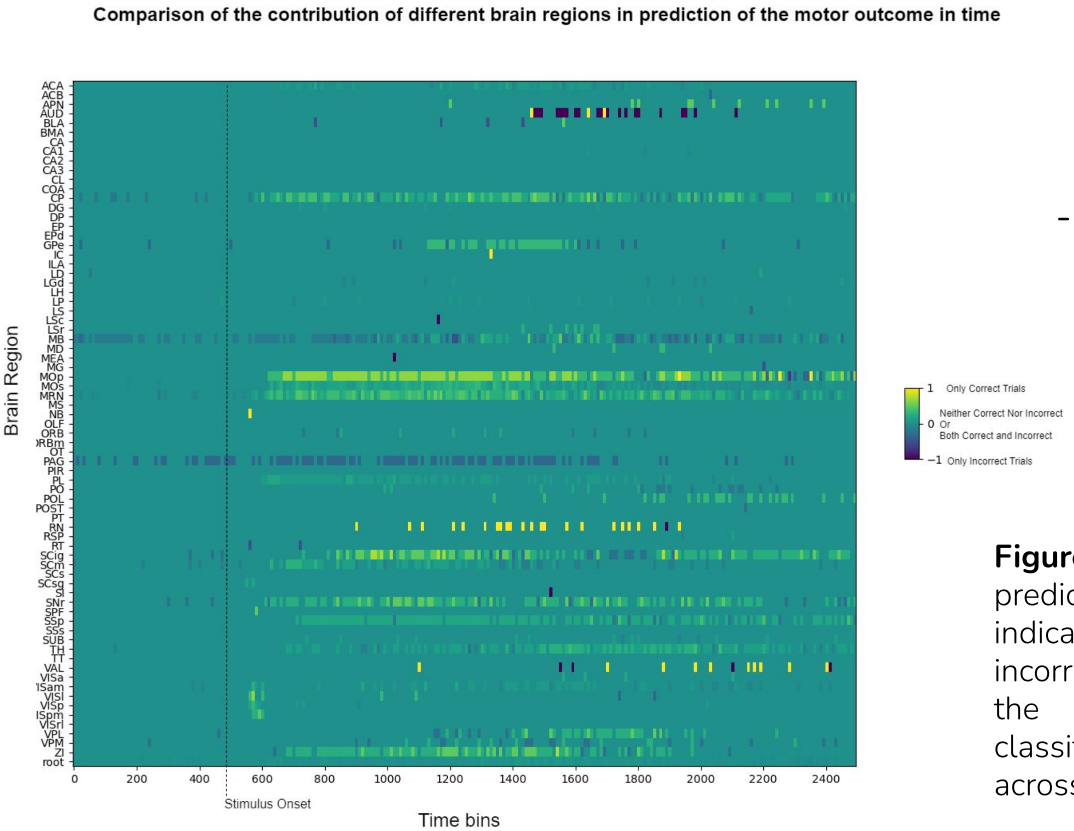
Results - Prediction of Motor Action

Prediction Accuracies by Region Across Time

Brain Region	Stimulus Onset	Avg Go Cue	500ms	1000ms	1500ms	2000ms
CA2	0.257539683	0.3630952	0.3313492	0.3198413	0.315873	0.4293651
CA3	0.335625551	0.3409947	0.3501647	0.3550374	0.3397752	0.3384357
DP	0.406706627	0.3845677	0.3602642	0.371655	0.3563248	0.3682995
GPe	0.31083176	0.4137392	0.4137665	0.4477196	0.3550522	0.3074478
IC	0.397809542	0.3731091	0.5425127	0.4675124	0.4137595	0.4295151
MOp	0.312583415	0.3983729	0.5682368	0.6082971	0.5417505	0.5801421
MOs	0.337836992	0.3832718	0.4313928	0.4399448	0.3942917	0.383863
MRN	0.357467215	0.4378713	0.4906969	0.4792813	0.4743755	0.4441904
MS	0.358034547	0.3159041	0.3820884	0.3832859	0.3531466	0.3292118
SCig	0.328142274	0.364649	0.5064823	0.5354378	0.5167732	0.4827208
VISp	0.33938268	0.4164072	0.3768474	0.3388653	0.3602055	0.3484667

Table 1. Prediction accuracies of the decoding model in sample areas. Time (in ms) denotes time after onset of stimulus.

Results - Predicting Motor Outcome



- Region Identification with thresholding

Figure 10. Contribution of different brain areas in predicting motor behaviour over the time. Values indicate which of the two conditions (correct and incorrect) is exclusively contributing to the prediction of the motor behaviour. Chance level in binary classification was set to 0.55%. Values are averaged across all mice and sessions.