Imagining what was there:

Looking at an absent offer location modulates neural response in orbito-frontal cortex.

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Introduction

For decision making tasks with reward gambling and sequential reward offer cues presentation, neurons in the orbito-frontal cortex (OFC) have been associated with the coding and maintenance of the estimated value of a firstly presented offer expected value (EV) so that it could be compared with the estimated value of a later presented one [1-4]. Importantly, it is yet to be assessed what is the role of sensory offer cues and their features, such as the spatial location and temporal order of offer cues presentation in neural firing. Our research aim is to combine the analyses of the role of task variables such as gambling probability and reward sizes with eye movement behavior and neural spiking activity simultaneously recorded in OFC during the execution of a two-alternative gambling task with sequential visual offer cues presentation.

Behavioral task

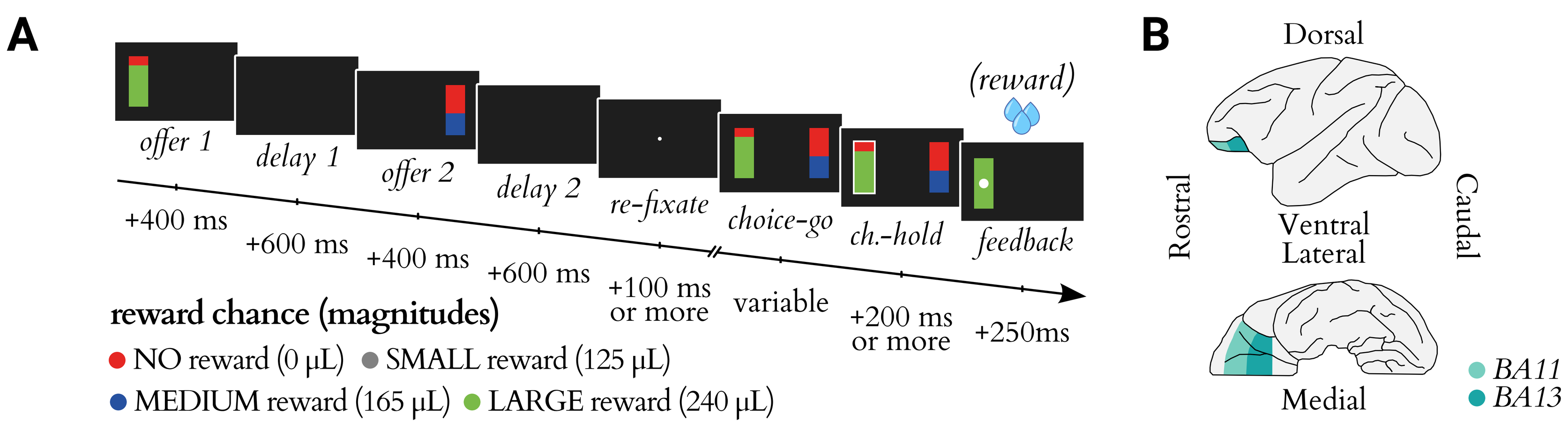

Figure 1. Behavioral Task, recorded brain areas. A) Two-alternative gambling task, sample configuration. Reward offers are sequentially cued by visual presentation of vertical bar stimuli on the two opposite sides of the screen. Stimuli colors either cue to a safe, small fluid reward (gray) or to risky rewards with size medium (blue) or large (green). Reward magnitudes were pseudo-randomized across trials. Risky reward probabilities were continuous random variables drawn from uniform distributions. The height of risky offers cues indicates the probability of achieving reward. No reward probability is indicated by complementing offer bars with red color. **B)** Recorded areas: Brodmann Areas 11 (BA11) and 13 (BA13), shown in the anatomical sketch redrawn from Mansouri et al., 2014[5]. Two adult male rhesus macaques (*Macaca mulatta*) served as subjects. All procedures were approved by the University Committee on Animal Resources at the University of Rochester or at the University of Minnesota, designed and conducted by T.C.-P., M.Z.W. and B.H. in compliance with the Public Health Service's Guide for the Care and Use of the Animals.

Results

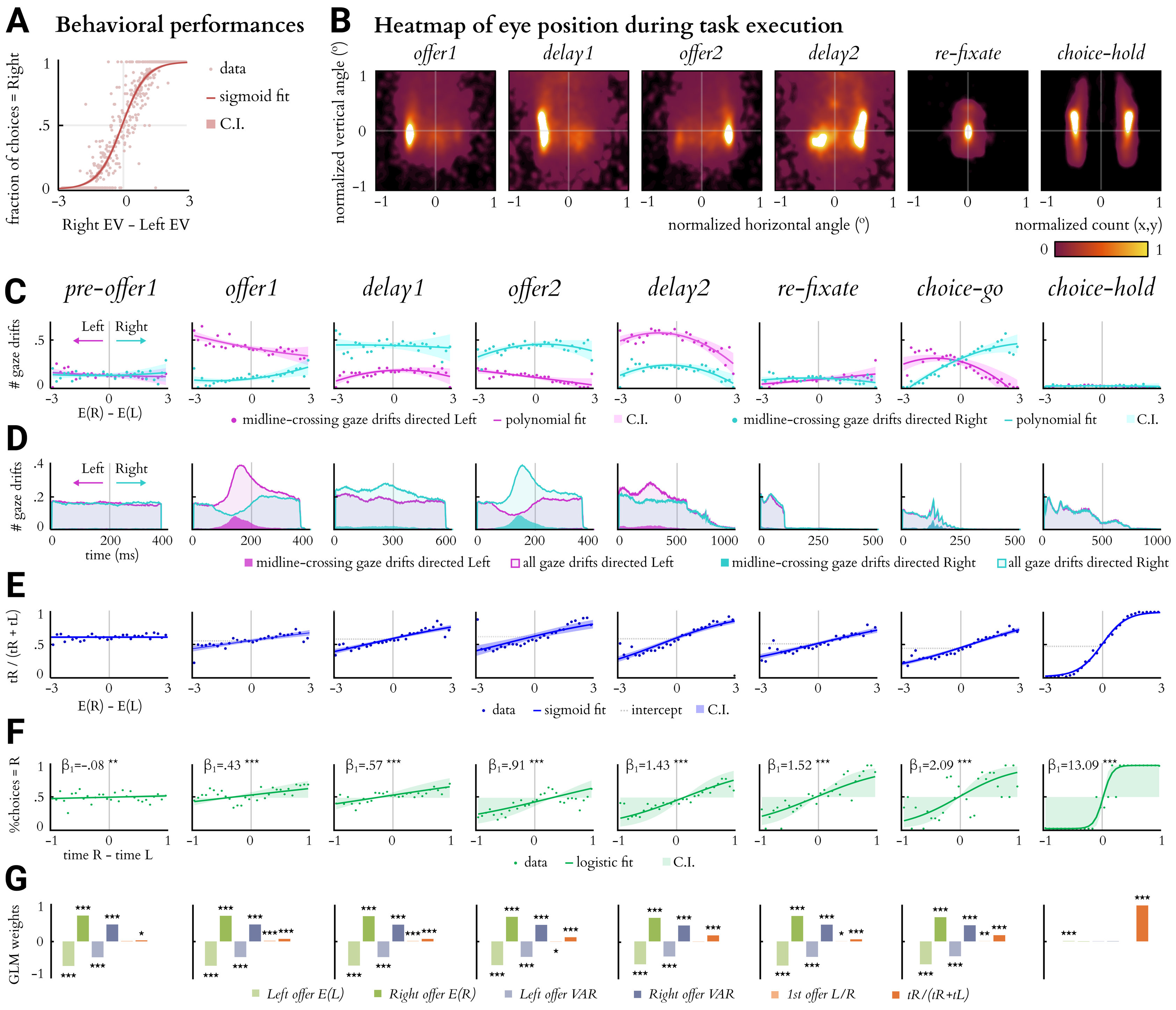

Figure 2. Behavioral data analyses. A) Behavioral task execution performances: chosen offer side vs E.V. difference (*E(R) - E(L)*). **B)** Heatmaps of eye position during task execution, smoothed with Gaussian filter with sigma = 5 bins. **C)** Screen midline crossing saccades labelled by direction. Solid lines: second order polynomial fit; shaded areas 95% Confidence Interval (C.I.). **D)** Time histograms of saccades occurrence labelled by direction (Solid areas: midline-crossing gaze drifts only; shaded areas: all gaze drifts). **E)** Fraction of time looking at Right screen side (*tR*) vs EV difference (*E(R) - E(L)* binned at 0.05 nominal units: 1=small, 2=medium, 3=large reward). Solid lines: sigmoid fits; shaded areas: 95% C.I. **F)** Chosen offer vs difference in time spent looking at either screen side. Solid lines: logistic regression fits (*logit(fraction of choices = Right)* = $\beta_0 + (tR - tL)\,\beta_1$); **G)** Generalized Linear Model of the subject's choice (*logit(fraction of choices = Right)* = $w_0 + w_1\,E(L) + w_2\,E(R) + w_3\,VAR(L) + w_4\,VAR(R) + w_5\,order + w_6\,tR/(tR{+}tL)$). **A-G)** Data include 5971 trials correctly performed (2643 from subject 1, 3328 from subject 2). Pooling is made with reference to the first offer side: eye data in trials with first offer on the Right side are horizontally mirrored; *p<0.05, **p<0.01,***p<0.001.

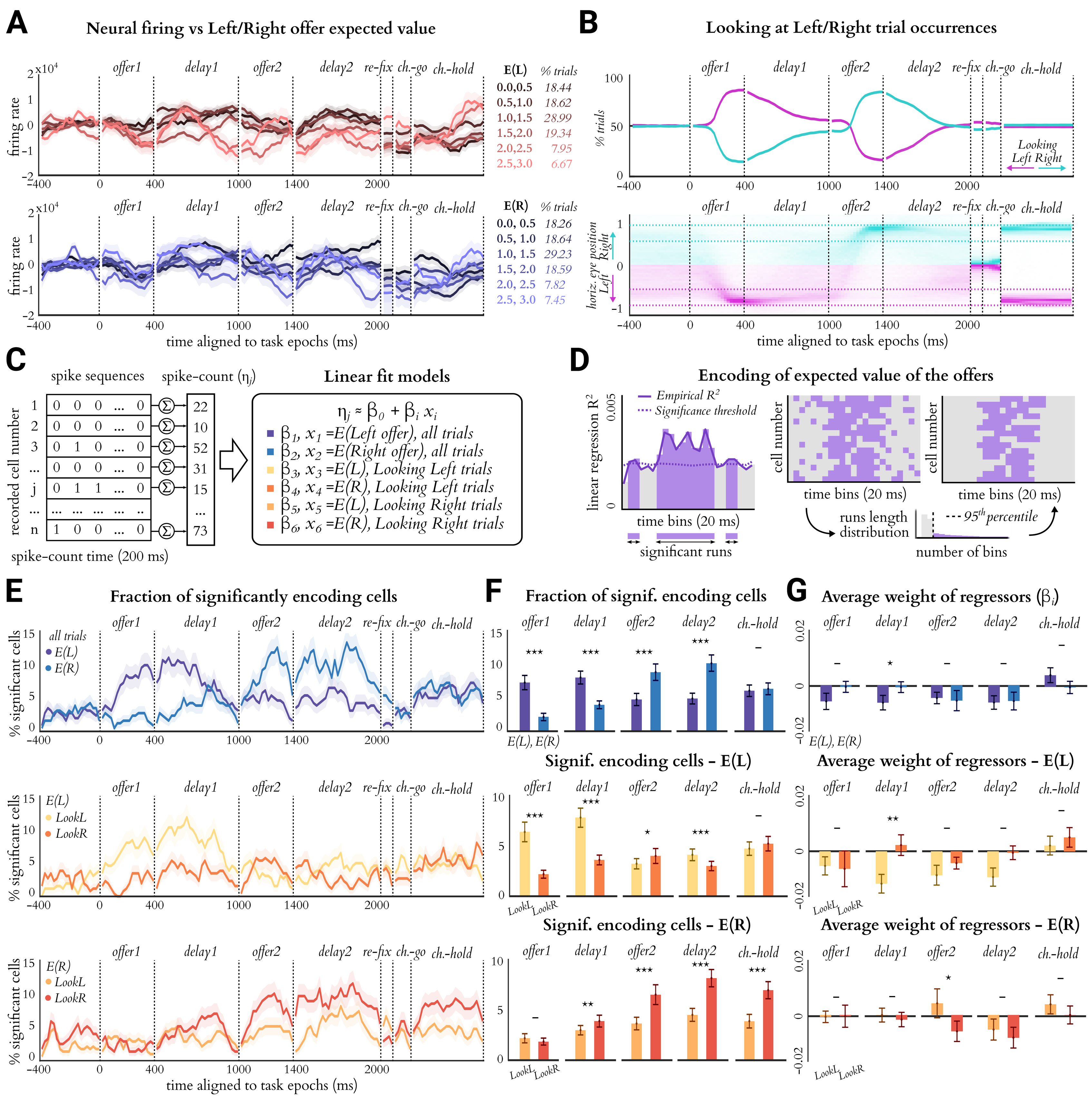

Figure 3. Analysis of OFC neural activity. A) Average neural firing vs Left (top) and Right (bottom) offer E.V., smoothed with a sliding mean filter covering 200ms at each 20ms. **B)** Occurrences of trials Looking at Left/Right screen side (top) and at binned horizontal eye coordinate (bottom) during task execution. **C)** Graphical sketch of the linear models for spike count and E(L), E(R). Regression is applied in 20ms bins and covers 200ms overlapping, causal time windows. The regression of E(L) and E(R) is repeated for trial pools where the subjects mostly looked L/R. **D)** Significance of the encoding of EVs in time bins. The empirical R^2 is compared with a significance threshold set as 95th percentile of R^2 for shuffled trial order. The length of significant (threshold crossing) time bins runs is assessed to the 95th percentile of significant run lengths for time-scrambled sequences[6-8]. **E)** Fraction of significantly encoding cells during task times: for E(L), E(R) including all trials (top), for E(L) in LookL vs LookR trials (middle) and for E(R) in LookL vs LookR trials (bottom). **F)** Same as E, but integrated in time for the most relevant task epochs. **G)** Average weight of the regression for E(L), E(R) including all trial (top), for E(L) in LookL vs LookR trials (middle) and for E(R) in LookL vs LookR trials (bottom). **A-G)** Eye data pooled with reference to the first offer on the L screen side (trials with first offer on R side are horizontally flipped). Neural units n=248 (163 from subect 1, 85 from subject 2), recorded in 4 sessions (2 for each subject). **F-G)** Significance assessed through non-parametric Wilcoxon signed rank tests: * is for p<0.05, ** is for p<0.01,*** is for p<0.001, - is for n.s.

Conclusions

- The fraction of time spent at either screen side is predictive of the chosen side;
- The gaze position is relevant in the process of encoding offer values: looking at either side yields stronger coding of the ipsi-later offer EV both during offer presentation and at delay times;
- Looking back at first offer presentation side during delay 2 times possibly allows to recall the value of previously shown offer, improving the strength of its encoding above the strength of encoding for most recent, contro-lateral offer.

References

[1] Strait, C.E., Blanchard, T.C. and Hayden, B.Y., 2014. *Reward value comparison via mutual inhibition in ventromedial prefrontal cortex.* Neuron, 82(6), pp.1357-1366.
[2] Rich, E.L. and Wallis, J.D., 2016. *Decoding subjective decisions from orbitofrontal cortex.* Nature Neuroscience, 19(7), pp. 973-980.
[3] Nogueira, R., Abolafia, J.M., Drugowitsch, J., Balaguer-Ballester, E., Sanchez-Vives, M.V. and Moreno-Bote, R., 2017. *Lateral orbitofrontal cortex anticipates choices and integrates prior with current information.* Nature Communications, 8(1), pp. 1-13.
[4] Hayden, B.Y. and Niv, Y., 2021. *The case against economic values in the orbitofrontal cortex (or anywhere else in the brain).* Behavioral Neuroscience, 135(2), p.192.
[5] Mansouri, F.A., Buckley, M.J. and Tanaka, K., 2014. *The essential role of primate orbitofrontal cortex in conflict-induced executive control adjustment.* Journal of Neuroscience, 34(33), pp.11016-11031.
[6] Cavanagh, S.E., Wallis, J.D., Kennerley, S.W. and Hunt, L.T., 2016. *Autocorrelation structure at rest predicts value correlates of single neurons during reward-guided choice.* elife, 5, p.e18937.
[7] Nichols, T.E. and Holmes, A.P., 2002. *Nonparametric permutation tests for functional neuroimaging: a primer with examples.* Human brain mapping, 15(1), pp.1-25.
[8] Butler, J.L., Muller, T.H., Veselic, S., Malalasekera, W.N., Hunt, L.T., Behrens, T.E. and Kennerley, S.W., 2021. *Covert valuation for information sampling and choice.* bioRxiv.

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