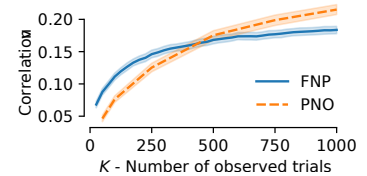


1 We thank all three reviewers for their valuable comments  
 2 and positive feedback. All reviewers agree that our ap-  
 3 proach addresses an important problem: real-time in-  
 4 ference of complex predictive neural models for online  
 5 closed-loop experiments. The reviewers find that our pa-  
 6 per “improve[s] the ability to estimate stimulus-response  
 7 models for neurons in the brain” (R1), that it “is a very  
 8 interesting paper and set of experiments” and its “use-case [...] compelling” (R2), and that our “approach is well  
 9 motivated and would address an important problem” (R4). Their main concerns are: 1 our experiments are only on  
 10 synthetic data (R1, R4), 2 our model is not compared to baseline models (R4), and 3 we need to present results about  
 11 training and prediction time (R2, R4). We are confident that we can address all concerns and that doing so improves  
 12 our results. We fit our Factorized Neural Processes (FNP) model to real neural responses from mouse V1. We find  
 13 comparable predictive accuracy to state-of-the-art models and critically—and by design—predicting the response  
 14 of unseen neurons is two-five orders of magnitude faster than using an optimization-based methodology. We will  
 15 include these results in the paper and improve the clarity of the presentation (R1, R2) with additional technical details in  
 16 supplemental materials. Because of the space limit, we can’t respond to all detailed concerns, but we will fix them.

Network	Time
FNP Optimization (once)	6 days on dual V100
FNP Inference for 1000 trials	<b>250 ms</b> (1080Ti)
PNO Readout only	~ 20 s (1080)
PNO CNN+Readout	~ 5 min (1080)
PNO + Hyperparameters	~ 12 h (1080)

17 **General motivation** Our goal is to rapidly infer a predictive model of newly  
 18 recorded neurons with minimal latency for online, closed-loop experiments. Our  
 19 envisioned use case (R4) is active learning of tuning properties where stimuli are  
 20 selected based on current estimates (and uncertainties, R2) of the tuning function to  
 21 better constrain the model and learn it more efficiently. This is not feasible online  
 22 with current models, even if just parts of the model are retrained (see 3). Prior  
 23 experiments with predictive models fit them to newly acquired neurons overnight and tested them the next day (e.g.  
 24 Bashivan2019 and Walker2019).



25 1 **Demonstration on real data** (R1, R4) We trained an FNP on 57,533 mouse V1 neurons responding to static scenes  
 26 collected across 19 different scans. We tested the  $K$ -shot predictive accuracy on 1000 randomly selected neurons  
 27 from a hold-out scan (i.e. never seen during training) with  $K$  up to 1000 natural images to infer the tuning properties  
 28 and predict responses to stimuli (a rapid network inference with no cell-specific optimization). In agreement with  
 29 synthetic data, the predictive accuracy improves rapidly with the first several hundred trials and continues to improve  
 30 with additional observations (see figure) establishing the utility of our method on real neural responses. The FNP also  
 31 generates realistic receptive field estimates.

32 2 **Comparison to baseline model** (R4) We now compare the performance of FNP (ours) to a SOTA model in the  
 33 style of Klindt2017, adapted for mouse V1, which we reference as Per Neuron Optimization (PNO). We trained it on  
 34 the responses of a single scan with 4,335 neurons to 5k natural scenes. Subsequently, we froze the core CNN and  
 35 fit a readout (linear+nonlinearity) to 1,000 new neurons on up to 1,000 images and measure the prediction accuracy.  
 36 Excitingly, FNP generalizes well to new neurons and with 1k images is almost as accurate as PNO (which is optimized  
 37 for those individual cells), and even *outperforms* it for smaller numbers of observations (see figure). Importantly, this is  
 38 achieved with massive improvements in run-time (see 3).

39 3 **Long training time** (R2, R4) We feel that there might have been a misunderstanding and we will make this more  
 40 clear in the paper: FNP needs to be trained *only once* using all previously recorded data (see 1). During experiments, a  
 41 predictor is obtained for newly acquired neurons with a nearly instant, single pass through the FNP. This takes only  
 42 250ms (for 1k responses) compared to optimization which ranges from ~20s (if only fitting the readout) to ~12h  
 43 (to optimize hyperparameters as we currently do in experiments). We summarize training times in the above table.  
 44 Thus getting a predictor with an FNP is two-five orders of magnitude faster, enabling real-time predictions. This is not  
 45 possible with existing methods (R4). Thus our approach allows inferring updated neural response properties within the  
 46 time of a single stimulus presentation.

47 **Other** (R2)  $q(z|s)$  is a variational approximation to  $p(z|s)$ ; **Two-stage method of ref[6]** is also optimization based;  
 48 **Eqn 1** integration is approximated by a single sample using the reparameterization trick (c.f. Kingma 2015), MLE is not  
 49 easy in deep learning; **sub-pixel interpolation** makes the loss differentiable for optimization (c.f. Spatial Transformer  
 50 Networks); **X-axis** corresponds to real trials (as above). **Section 3.3**  $\mathbb{R}^{H \times W \times C}$  is an image with  $C$  channels after  
 51 passing through the convolution and  $H \times W$  refers to the spatial dimensions. It is then combined (non-linearly) with  
 52 the responses to predict the location. Response units can be fluorescence (as above) or spike counts (see simulations)  
 53 **Uncertainty** is currently only used as a tool for training, we imagine using entropy to drive stimulus selection; **Cell**  
 54 **types**: good point, we did not want to emphasize categories, continuum is also possible, will revise terminology; **Fig 2**  
 55 **& LL** see 1, 2 for real world example. **Complex cell RFs**: Correct! it looks opposite at times due to the random  
 56 phase shifts; **Code** was withheld for anonymity, will be released; **Broader impact** will be updated, good suggestions.