Bayesian nonparametric (non-)renewal processes for analysing neural spike train variability

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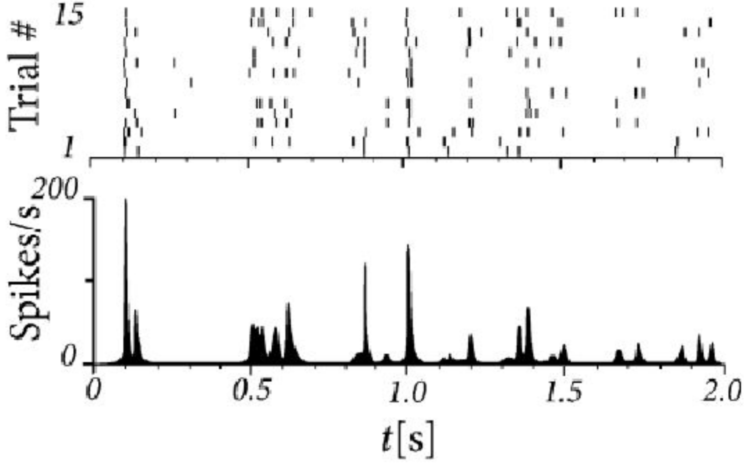
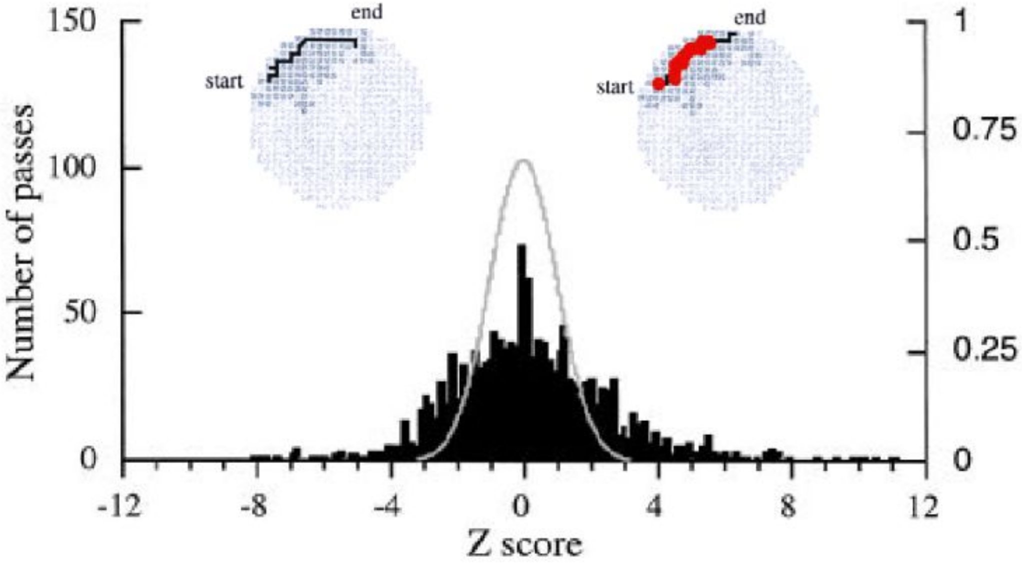
Neural variability

neural responses are variable

same for trial-free recordings, more involved to quantify variability



Gerstner et al. 2014

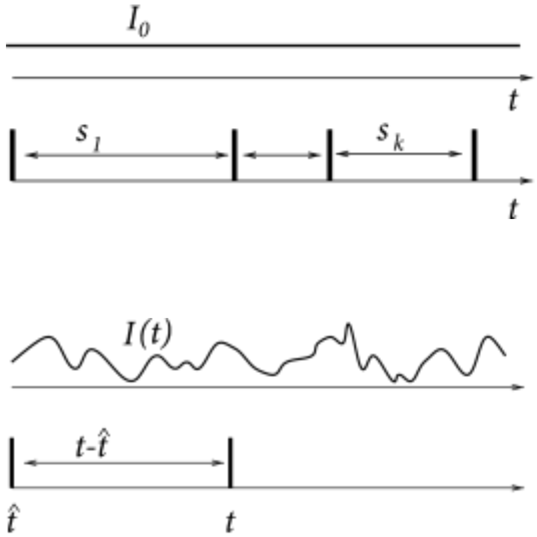


Fenton et al., PNAS 1998

Neural variability

stationary spike trains: use empirical estimators

nonstationary spike trains: need explicit model



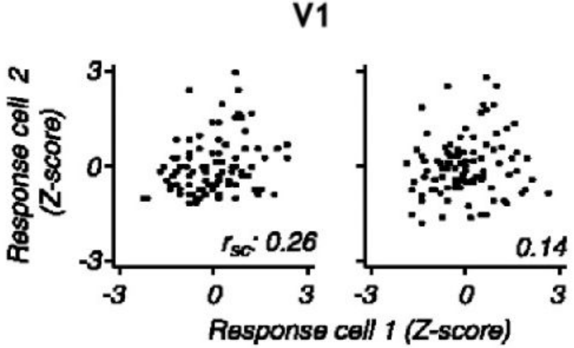
Not just noise?

simplest case: spike count analyses with trials

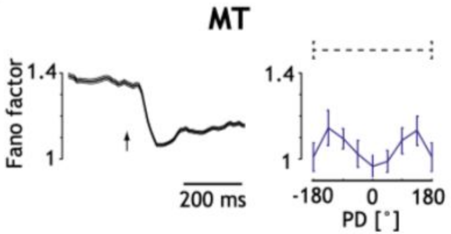
look at variance, not just the mean

nontrivial features of variability:
- large, richly patterned spontaneous activity
- structure noise correlations and shared variability
- controlled by stimuli

a feature, not a bug: signatures of Bayesian inference
(Ma et al. 2006, Orban et al. 2016)



Kohn et al., J Neurosci 2005



Churchland et al., Nat Neurosci 2010

Ponce-Alvarez et al., PNAS 2013

Current approaches

coarse-grain by temporal binning of spikes

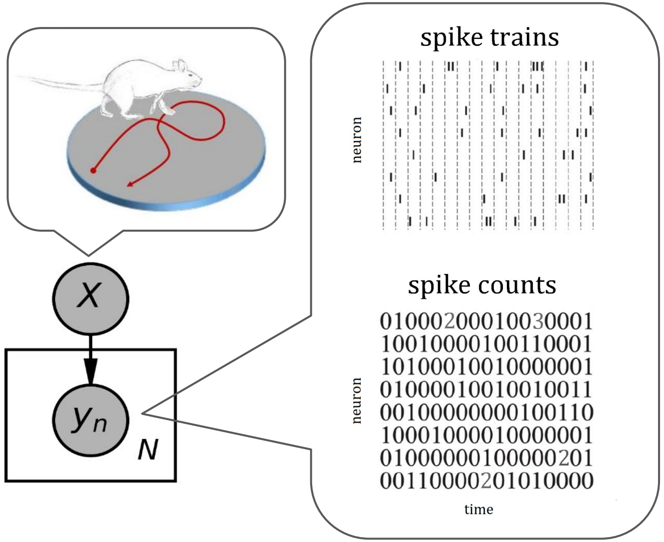
go beyond trial structure with model-based estimates

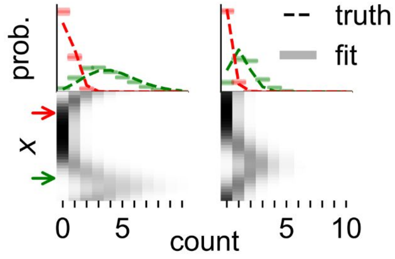
flexible count-based regression models:

- heteroscedastic noise models (Ghanbari et al. 2019)
- universal count models (Liu & Lengyel 2021)

analysis affected significantly by choice of bin size!

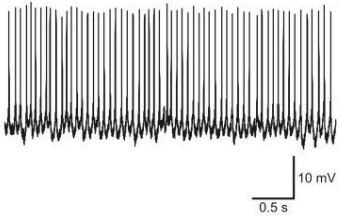
fundamentally, dealing with spike events

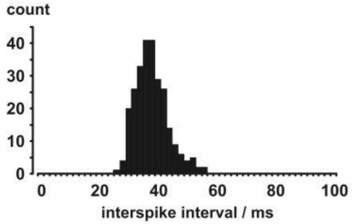




Current approaches

spiking variability, interspike interval (ISI) distribution

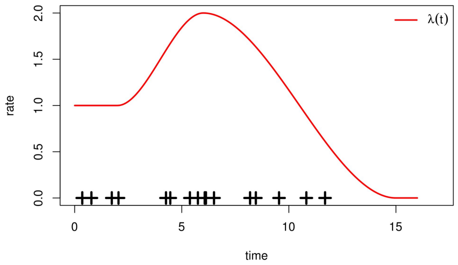




point process framework

conditional hazard function (CIF) $$\lambda(t|\mathcal{H}_t) = \lim_{\delta t \to 0} \frac{\mathbb{E}[N(t+\delta t) - N(t)|\mathcal{H}_t]}{\delta t}$$

modulation by external covariates $\lambda(t|\mathcal{H}_t, \boldsymbol{x}_{\leq t})$



constrain CIF for tractable inference:
- factorized modulation (Teh & Rao 2011)
- Markov renewal assumption (Brown et al. 2002)
- spike-history filters

limitations of existing methods:
- parametric constraints on spiking variability
- no flexible input-dependent modulation of spiking variability, i.e. ISI distribution shape

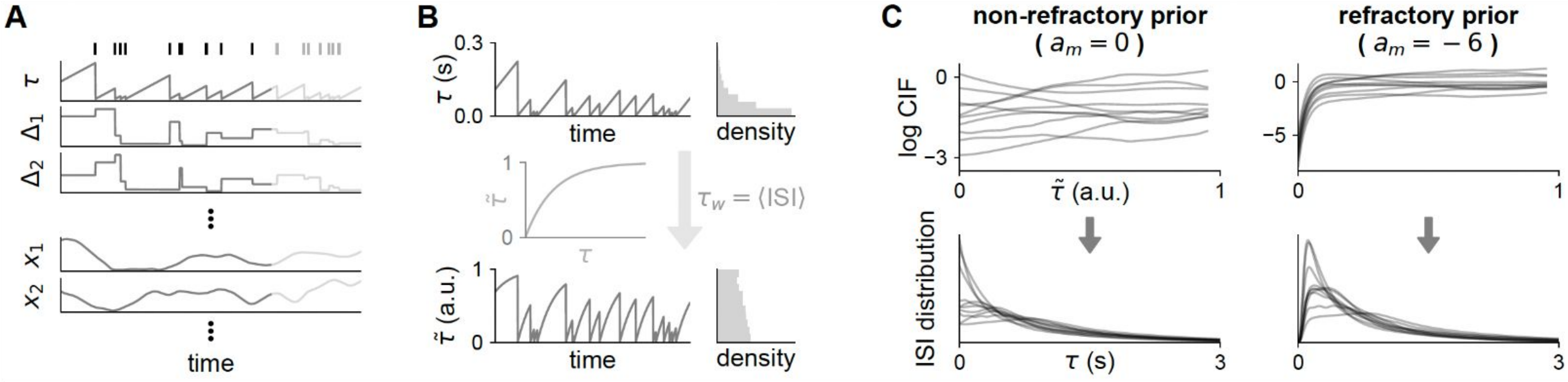
Generative model

Gaussian process prior over log CIF $f(\tau, \boldsymbol{x}_t) \sim \mathcal{GP}\left(m(\tau, \boldsymbol{x}), k_t(\tau, \tau') \cdot k_x(\boldsymbol{x}, \boldsymbol{x}')\right)$

inputs provide history dependence beyond renewal order (previous spike) $\log \lambda(t|\mathcal{H}_t, \boldsymbol{x}_t) = f(\tau, \boldsymbol{\Delta}_t, \boldsymbol{x}_t)$

prior over CIF ⇔ prior over conditional ISI distributions $g(\tau|\boldsymbol{\Delta}_t, \boldsymbol{x}_{(t_i,t]}) \propto \lambda(t|\mathcal{H}_t, \boldsymbol{x}_t) \cdot e^{-\int_{t_i}^{t} \lambda(t'|\mathcal{H}_{t'}, \boldsymbol{x}_{t'})\, \mathrm{d}t'}$

nonparametric non-renewal (NPNR) process



Inference

variational approach, time discretization

posterior flexibly captures modulation by time-varying covariates

posterior over modulated ISI distributions, ISI moments $\mathbb{E}_{g(\tau)}[\tau^m] = \int_0^\infty g(\tau)\,\tau^m\,\mathrm{d}\tau$

model-based estimates of spike train statistics:
- firing rate as reciprocal mean ISI $1/\mathbb{E}[\tau]$
- coefficient of variation (CV) $\sqrt{\mathrm{Var}[\tau]}/\mathbb{E}[\tau]$

requires evaluating GP posterior at many locations (Wilson et al. 2020)

Goodness-of-fit for point processes

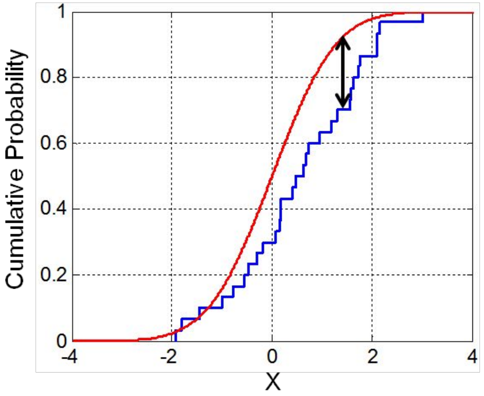
time-rescaling

$$\bar{t}(t) = \int^{t} \lambda(t'|\ldots)\,\mathrm{d}t'$$

Kolmogorov-Smirnov goodness-of-fit test

$$q(\bar{\Delta}) = F_{\exp}(\bar{\Delta}) = 1 - e^{-\bar{\Delta}}$$

$$T_{\mathrm{KS}} = \max_{q} |F(q) - q|$$

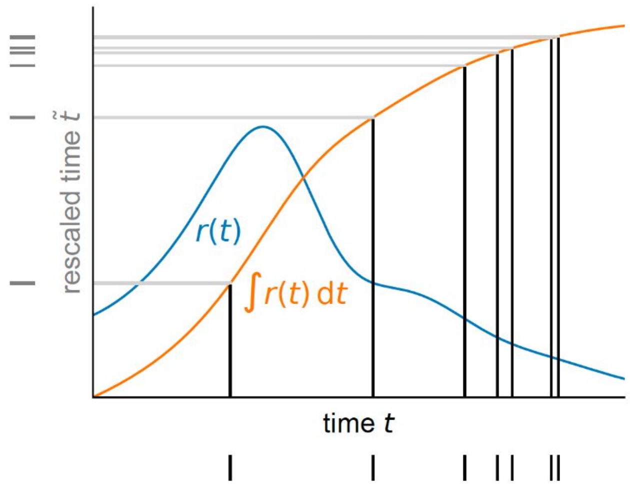


Validation on synthetic data

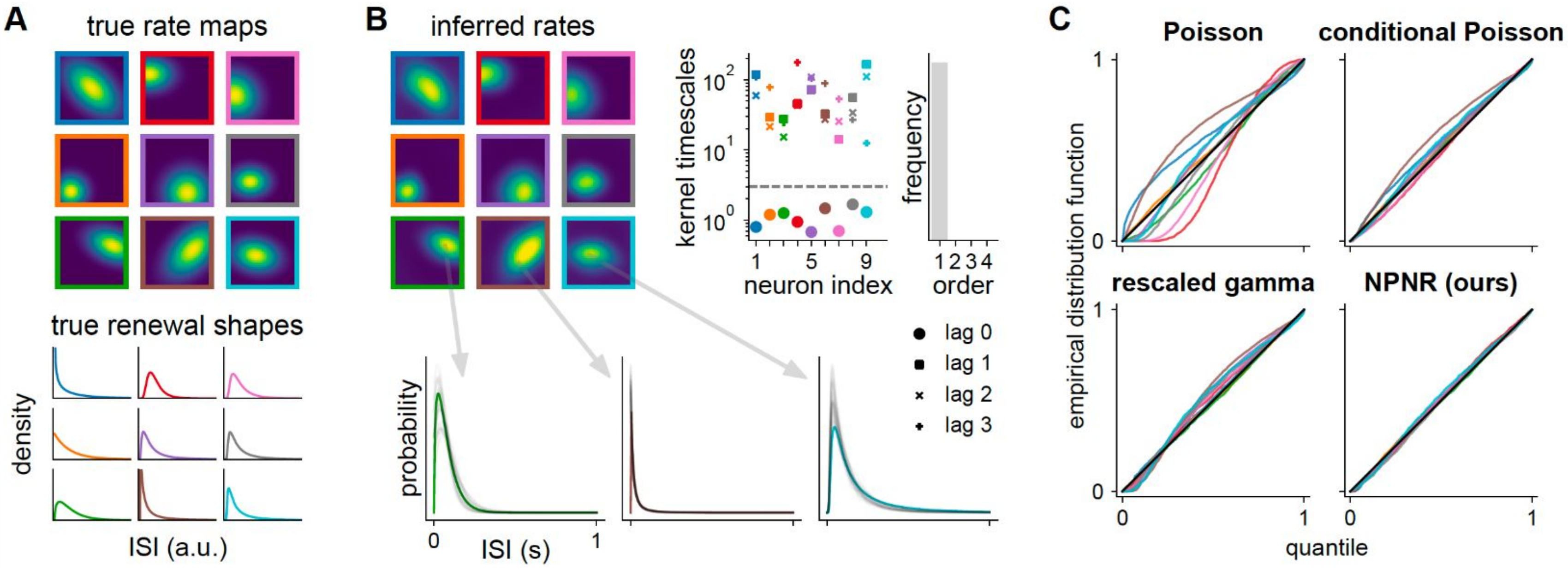
rate-rescaled renewal process

generative procedure:

- sample events from homogeneous renewal process
- compute rate as function of time
- compute cumulative rate
- obtain rescaled event times

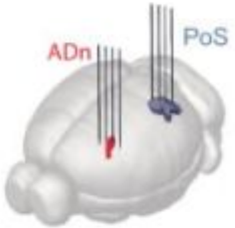


Validation on synthetic data

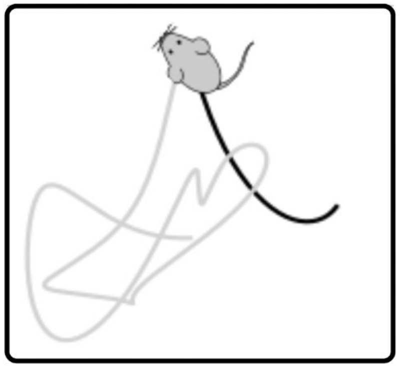


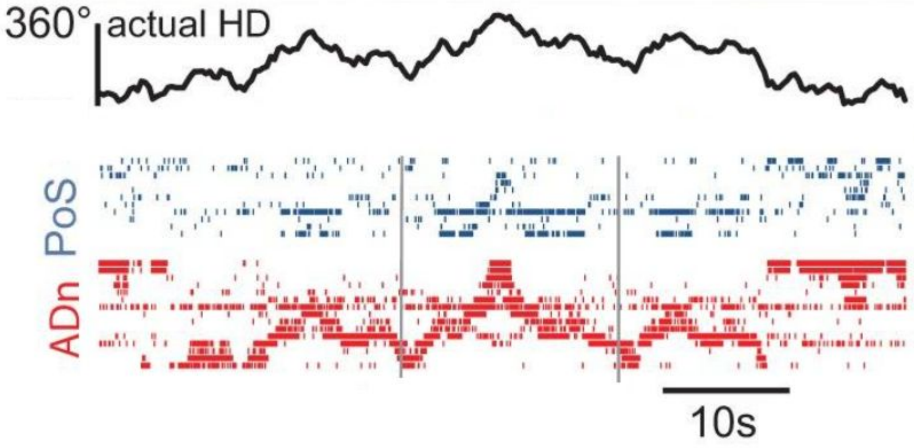
Mouse head direction cells

recording from antero-dorsal subnucleus (ADn) and postsubiculum (PoS)
(Peyrache et al. 2015)



freely moving chasing food pellets





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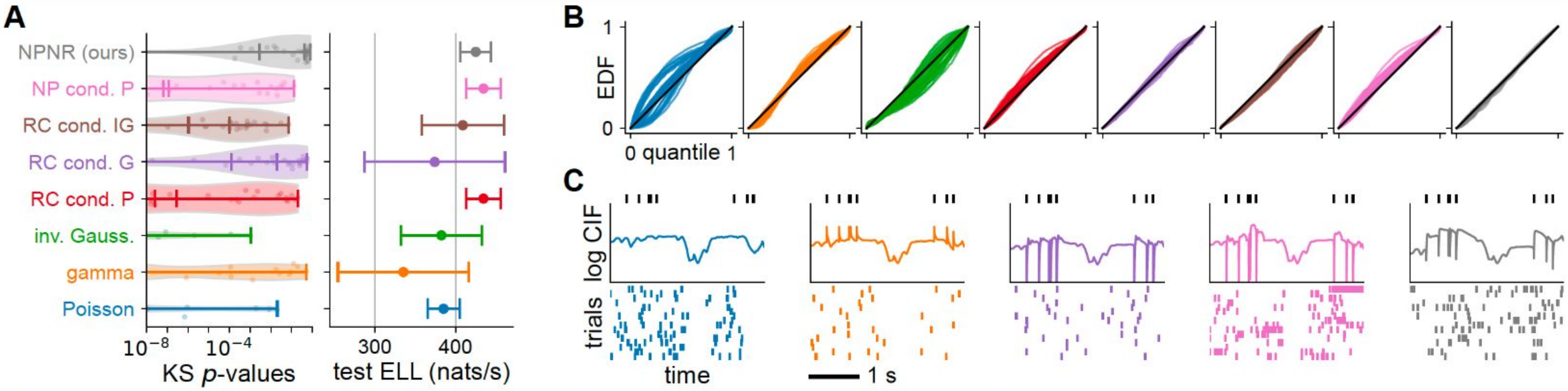

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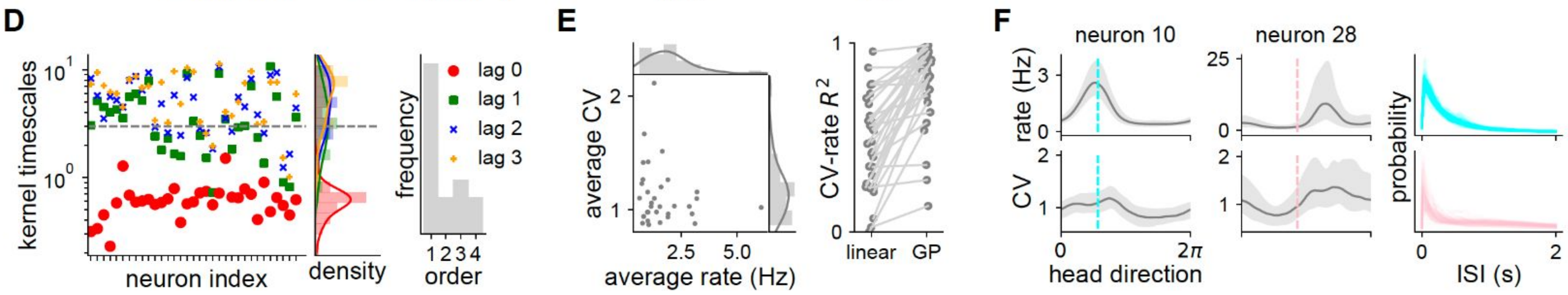
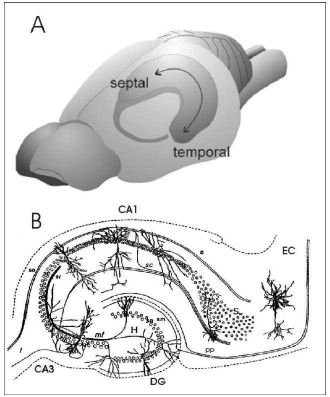
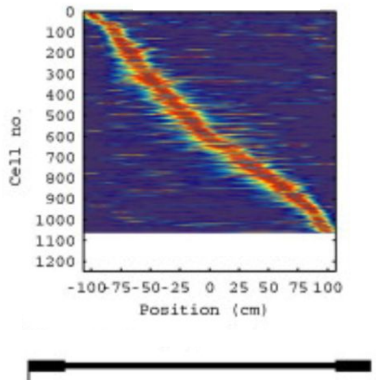


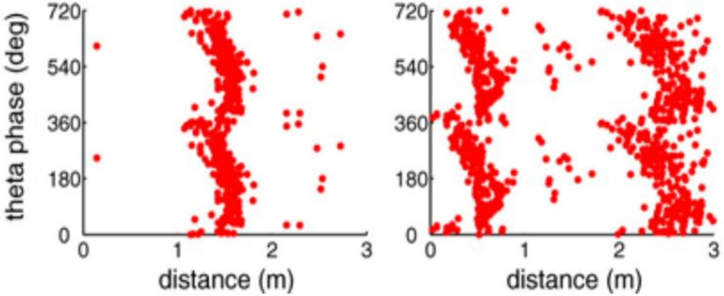
Rat place cells

recording from CA1 (Mizuseki et al. 2009)

running along linear track







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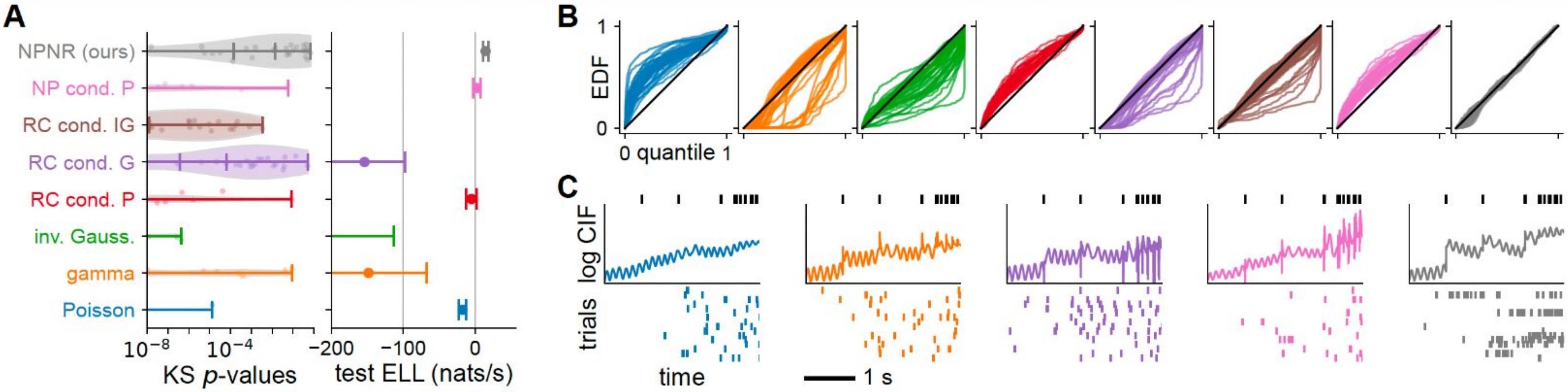

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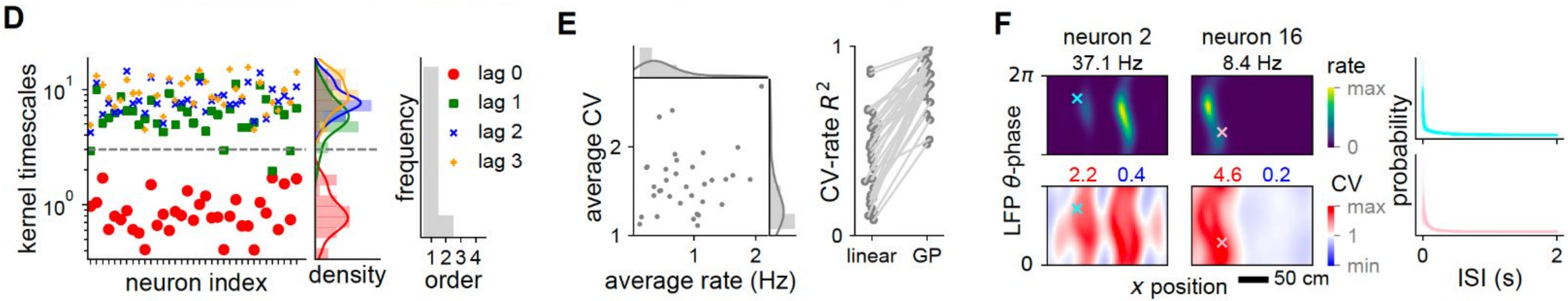

Summary

nonparametric non-renewal processes for neural spike train data

analysis of neural data:

- both over- and underdispersed regimes
- variability tends to increase with firing rate
- firing rate and CV can be decoupled

further work:

- latent variable modeling
- additional spike train statistics

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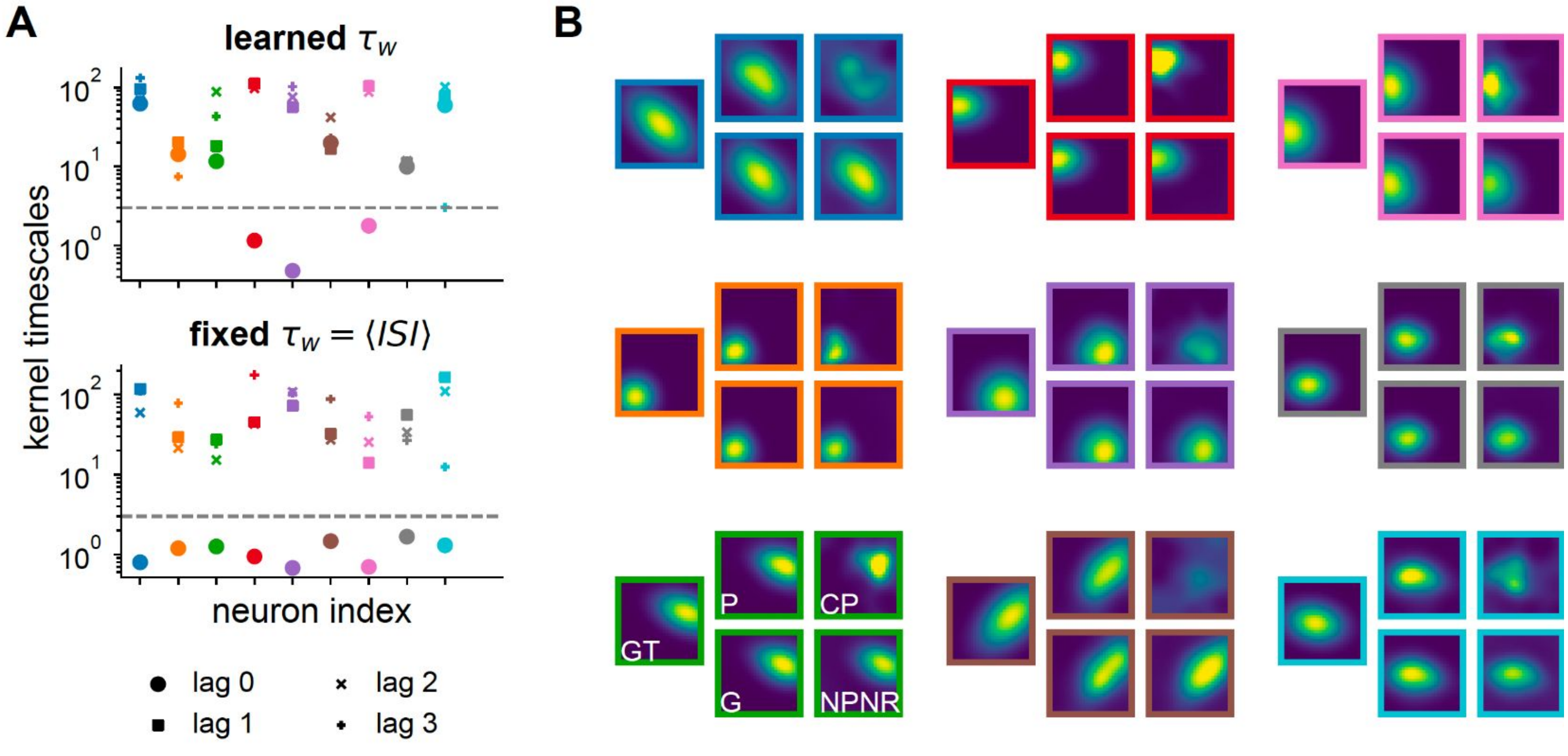
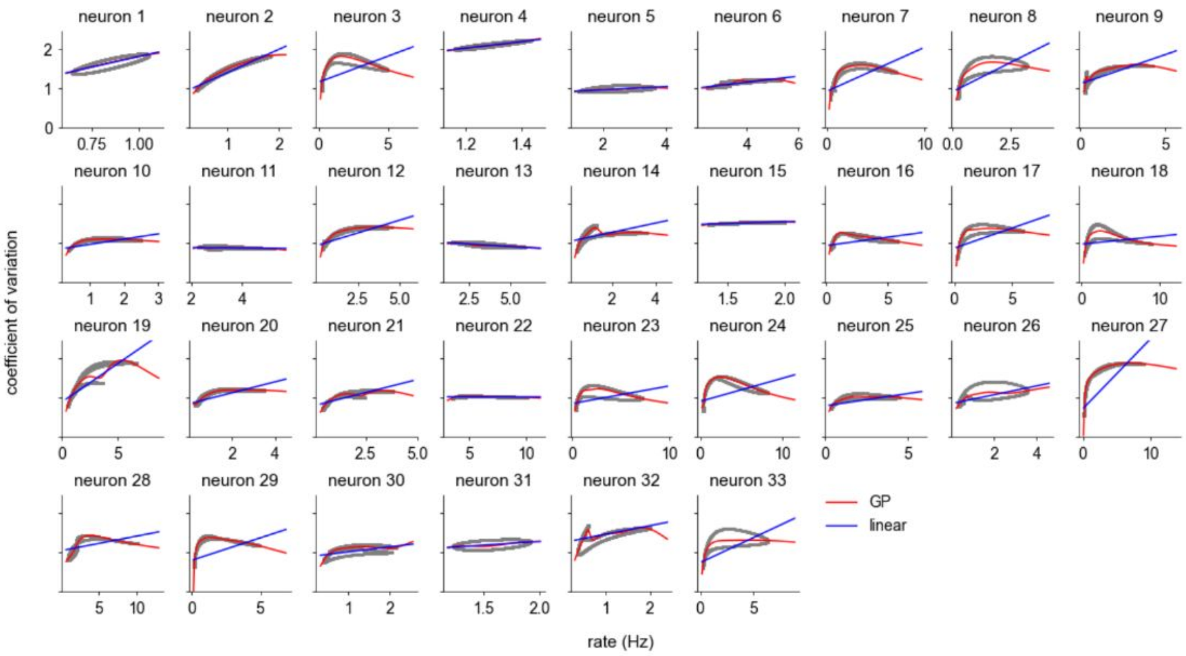
Additional validation results



Additional head direction data analysis



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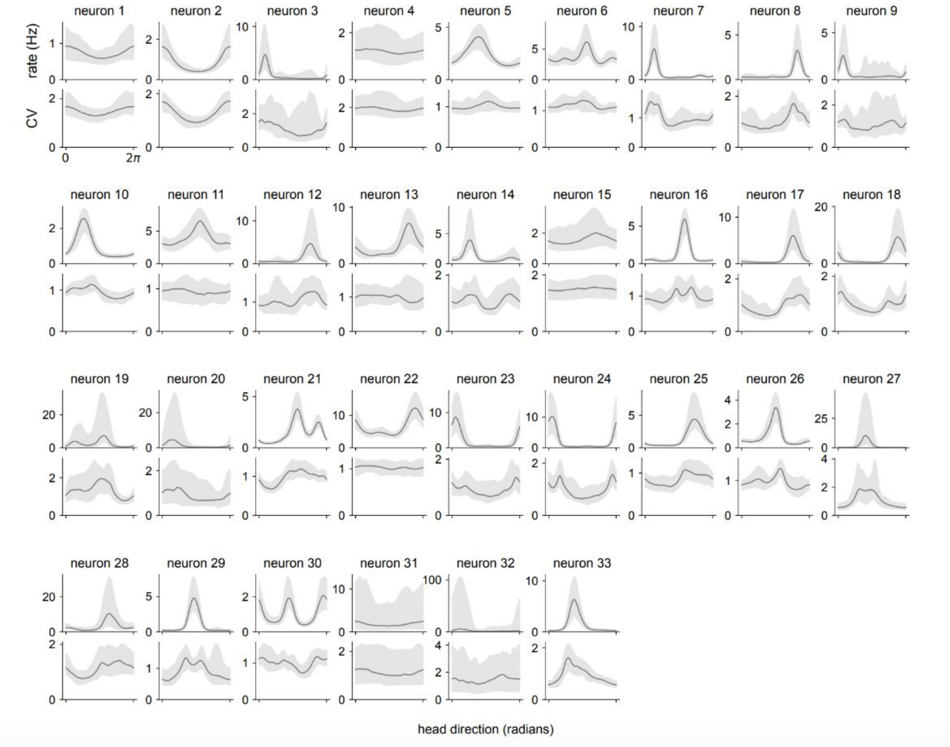
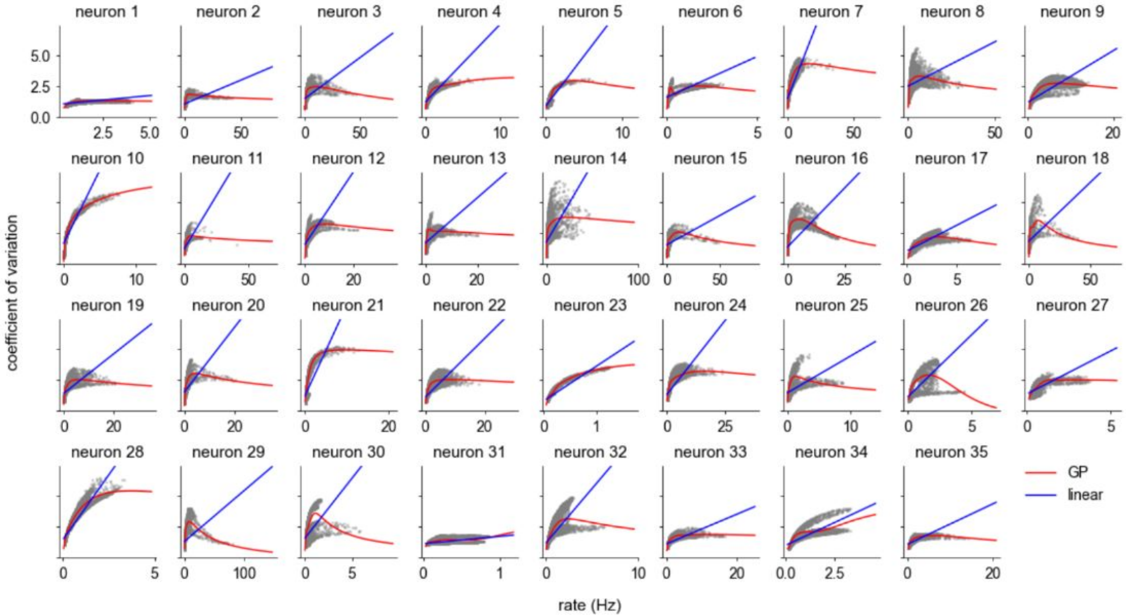


Additional place cell data analysis



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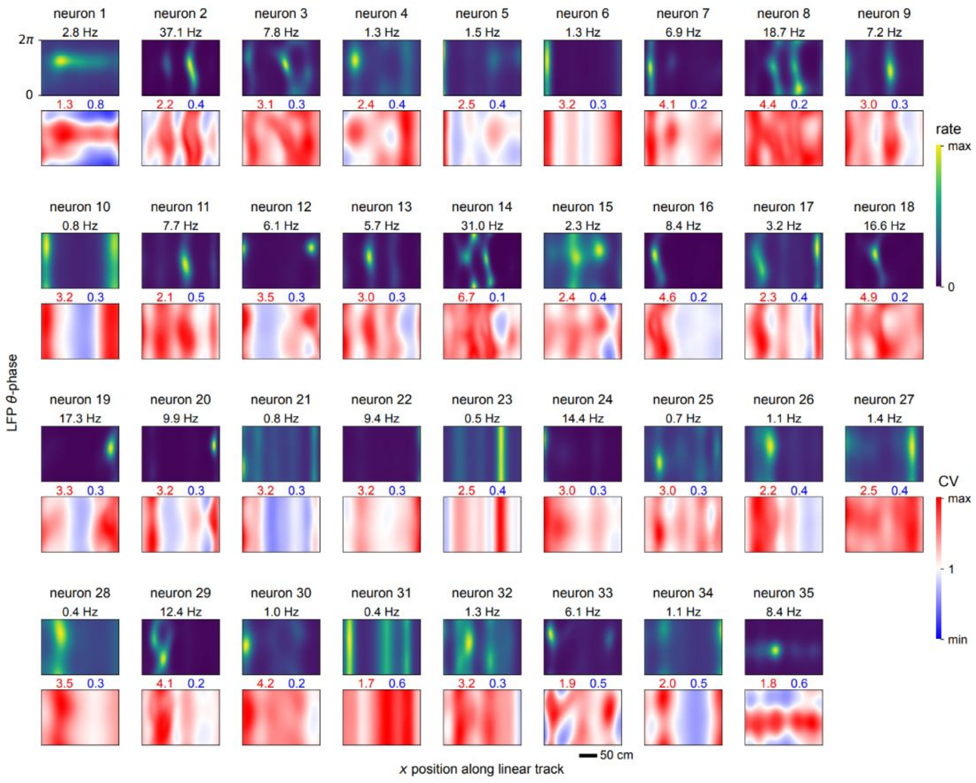

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