Instantaneous firing rate and counting statistics of spike trains

Lubomir Kostal

Institute of Physiology CAS, Prague, Czech Republic

- Spike train as a point process
- **Instantaneous interspike intervals**
- Results (*work in progress*)
    1. Estimation of firing rate
    2. Estimation of spike train variability
- Other possible applications...

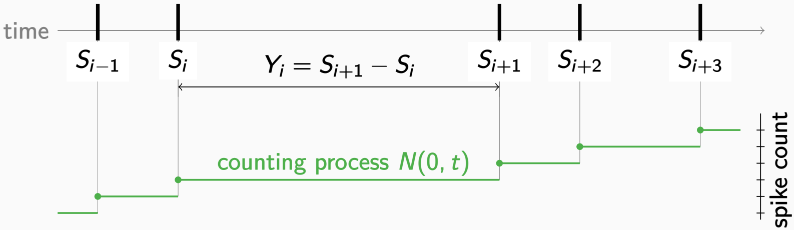
Conclusions

- ISIs observed at given reference time have *different* statistics than *sequential* (standard) ISIs.
- Possibility to estimate classical characteristics (firing rate, variability) in a novel way.

Spike train as a point process

Spike train as a Point Process (PP)

Spike times S_i, interspike intervals (ISI) Y_i, counting process $N(0, t)$



- Assume time $t = 0$ is *unrelated* to spike times
- Equivalent description: $\{S_i \leq t\} = \{N(0, t) \geq i\}$, $i = 1, 2, \ldots$

Point process intensity and firing rate

- Conditional *intensity* depends on the PP history up to time t (instantaneous firing rate)

$$\lambda(t) = \lim_{\varepsilon \downarrow 0} \frac{\mathrm{E}[N(t, t+\varepsilon)]}{\varepsilon}$$

- The mean *firing rate* in 'window' w

$$\nu(t, w) = \frac{\mathrm{E}[N(t, t+w)]}{w}$$

- Without detailed description of the PP: $\lambda(t) \overset{?}{\leftrightarrow} \nu(t, w)$
- Let's make additional assumptions . . .

Renewal processes (ordinary$^{i)}$ and in equilibrum$^{ii)}$)

i) Assume $\{Y_1, Y_2, \dots\}$ is i.i.d., $Y \sim f_Y(y)$, then[1] for any t:

$$\frac{1}{\mathrm{E}(Y)} = \lim_{w \to \infty} \nu(t, w)$$

ii) For arbitrary t: $\{S_i - t, Y_{i+1}, Y_{i+2}\}$ is not stationary, but $\lambda = \lambda(t)$, $\nu(w) = \nu(t, w)$ and for all $w > 0$

$$\lambda = \frac{1}{\mathrm{E}(Y)} = \nu(w)$$

[1] Cox, D. R. & Lewis, P. A. W. (1966) *The statistical analysis of series of events*, Whistable: Latimer Trend and Co. Ltd.

Temporal and *counting* descriptions (renewal PP)

- Let $p_n(w) = \Pr\left(N(t, t+w) = n\right)$, $n = 0, 1, 2...$, then[2]

$$p_0(w) = \mathcal{L}^{-1}\left[\frac{1}{s} - \frac{1 - \mathcal{L}[f_Y](s)}{s^2\,\mathrm{E}(Y)}\right](w)$$

$$p_n(w) = \mathcal{L}^{-1}\left[\frac{\left(1 - \mathcal{L}[f_Y](s)\right)^2\left(\mathcal{L}[f_Y](s)\right)^{n-1}}{s^2\,\mathrm{E}(Y)}\right](w), \quad n \geq 1$$

- Higher moments[3] of $N(t, t+w)$ and Y? (*later: Fano factor*)

$$\mathrm{Var}[N(t, t+w)] \overset{w\to\infty}{\approx} \frac{\mathrm{Var}(Y)}{\mathrm{E}(Y)^3} w + \frac{1}{2}\left(1 + \frac{\mathrm{Var}(Y)}{\mathrm{E}(Y)^2}\right)^2 - \frac{\mathrm{E}(Y^3)}{3\,\mathrm{E}(Y)^3}$$

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[2] Jewell, W. S. (1960) ‘The properties of recurrent-event processes’, *Operation Res.* 8, 446–472

[3] Cox, D. R. (1962) *Renewal Theory*, London: Methuen and Co. Ltd.

Instantaneous firing rate

- Calculating the true firing rate (PP *intensity*) from the general (non-stationary) temporal description is difficult
- *Instantaneous*[4] firing rate: inverse ISI, $1/Y$ (correct dimension)

[4] Bessou, P., Laporte, Y. & Pagés, B. (1968) 'A method of analysing the responses of spindle primary endings to fusimotor stimulation', *J. Physiol.* 196, 37–75

Instantaneous firing rate

- Calculating the true firing rate (PP *intensity*) from the general (non-stationary) temporal description is difficult
- *Instantaneous*[4] firing rate: inverse ISI, $1/Y$ (correct dimension)
- **However**[5]: *mean* instantaneous firing rate (renewal PP):

$$\boxed{\mathrm{E}\left(\frac{1}{Y}\right) \geq \frac{1}{\mathrm{E}(Y)}}$$

[4] Bessou, P., Laporte, Y. & Pagés, B. (1968) 'A method of analysing the responses of spindle primary endings to fusimotor stimulation', *J. Physiol.* 196, 37–75

[5] Lansky, P., Rodriguez, R. & Sacerdote, L. (2004) 'Mean Instantaneous Firing Frequency Is Always Higher Than the Firing Rate', *Neural Comput.* 16, 477–489

Instantaneous interspike intervals

Unifying the *steady state* and *instantaneous* firing rate

- Observe single or parallel spike trains (at some time t_0).
- ISIs described by $Y \sim f_Y(y)$: always from "spike to spike", i.e., t_0 corresponds to a spike!
- However, spike trains are often modulated by external stimulus – t_0 must be unrelated to spikes $\Rightarrow$ *external/laboratory* time.

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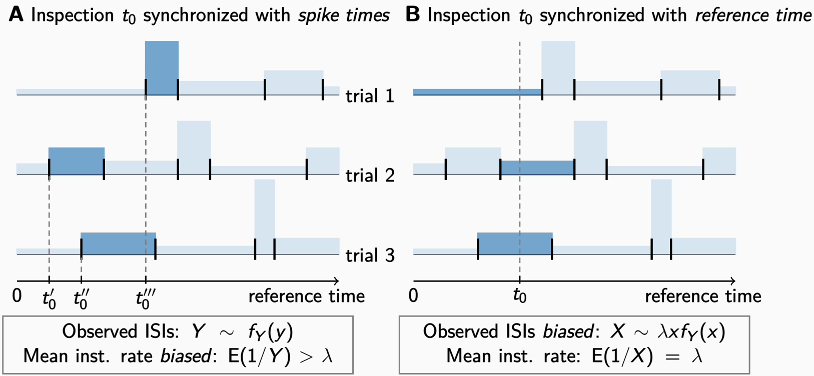
- **Therefore**

$$\mathrm{E}\left(\frac{1}{X}\right) = \lambda = \frac{1}{\mathrm{E}(Y)}$$

Instantaneous interspike intervals[6] (*summary*)



[6] Kostal, L., Lansky, P. & Stiber, M. (2018) 'Statistics of inverse interspike intervals: the instantaneous firing rate revisited', *Chaos* 28, 106305

Estimation of firing rate from instantaneous ISIs

Non-parametric estimator based on instantaneous ISIs X_i

- Estimate the instantaneous firing rate λ (assume renewal PP)
- Immediate consequence of $\lambda = \mathrm{E}(1/X)$: *moment estimator*

$$\widehat{\lambda}_m = \frac{1}{n}\sum_{i=1}^{n}\frac{1}{X_i}, \quad \mathrm{E}(\widehat{\lambda}_m) = \lambda, \quad \mathrm{MSE}(\widehat{\lambda}_m) = \frac{\lambda\,\mathrm{E}(1/Y) - \lambda^2}{n}$$

- Mom. est. not efficient[7], e.g., $\lim_{n\to\infty} n\,\mathrm{MSE}(\widehat{\lambda}_m) > 1/I_F(\lambda)$
- Furthermore $E(1/Y) = \infty$ if $f_Y(0) > 0$ (e.g., Poisson[8])

[7] Kostal, L. (2023) 'Estimation of firing rate from instantaneous interspike intervals', (in preparation)

[8] Lansky, P., Rodriguez, R. & Sacerdote, L. (2004) 'Mean Instantaneous Firing Frequency Is Always Higher Than the Firing Rate', *Neural Comput.* 16, 477–489

Maximum likelihood estimator (I)

- MLE efficient under mild conditions ($\rightarrow$ mismatched est.)
- Let $X \sim f_X(x;\lambda) \equiv \lambda x f_Y(x)$, then

$$\widehat{\lambda}_{ML} = \arg\max_{\lambda} \sum_{i=1}^{n} \log f_X(x;\lambda)$$

- **Poisson process** ISIs Y: $f_Y(y) = \lambda \exp(-\lambda y)$
- MLE can be derived[9] and un-biased $\forall n$, $\mathrm{E}(\widehat{\lambda}_{ML}) = \lambda$

$$\widehat{\lambda}_{ML} = \left(\frac{1}{2n-1}\sum_{i=1}^{n} X_i\right)^{-1}, \quad \mathrm{MSE}(\widehat{\lambda}_{ML}) = \frac{\lambda^2}{2n-2}, n \geq 2$$

[9] Kostal, L. (2023) 'Estimation of firing rate from instantaneous interspike intervals', (in preparation)

Maximum likelihood estimator (II)

- MLE can be derived also for, e.g., γ p.d.f. of Y
- Useful case: Poisson process with refractory period τ_r ($< 1/\lambda$)

$$\widehat{\lambda}_{ML} = \frac{\mu + 2\tau_r - \sqrt{\mu^2 + 4\mu\tau_r - 4\tau_r^2}}{2\tau_r^2}, \quad \mu = \frac{1}{n}\sum_{i=1}^{n} X_i$$

- Biased, no closed form for $\mathrm{Var}(\widehat{\lambda}_{ML})$
- From data: $\widehat{\tau}_r = \min X_i$ (*mismatched if* $\tau_r = 0$)

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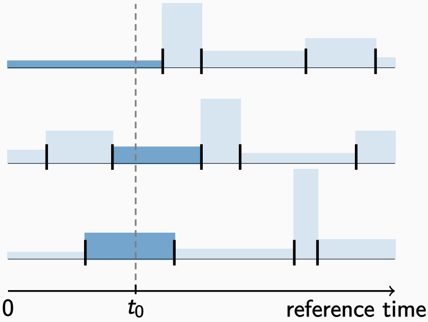
- Renewal PP vs. *non-stationary* spike trains
  Can we use estimators based on X_i?

Estimation under time-dependent $\lambda(t)$

- Estimate $\lambda(t)$ at $t = t_0$



- Eqs. derived under *renewal PP* $\rightarrow$ can be used more generally?
- $\widehat{\lambda}_{ML}$ is "*self-adaptive*" (time scale automatically given by $\langle X_i \rangle$)
  - no optimization, no additional parameters

Preliminary comparison of different estimators

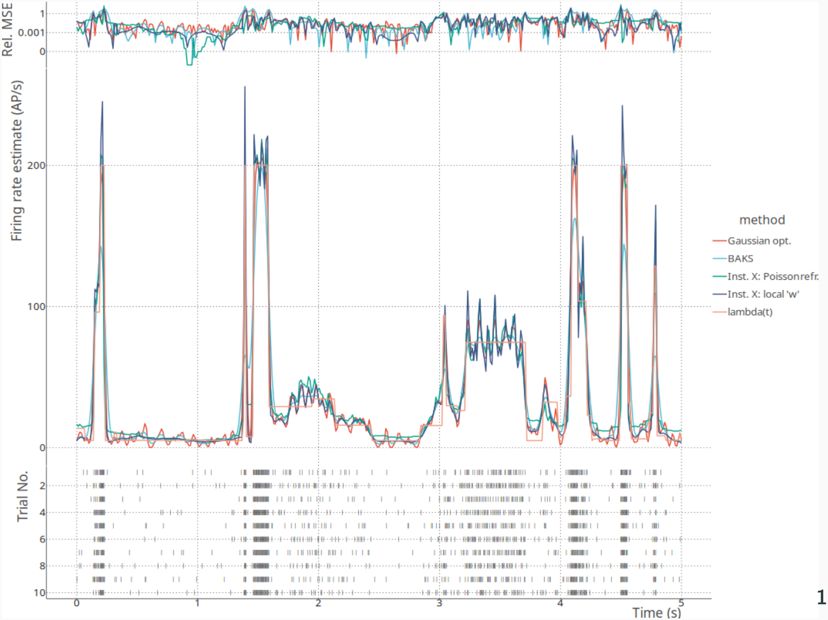
- Most methods *pool* spike train data (across trials)
  - Binning, kernel ... binwidth *guess* (20ms, 50ms, ...)
  - Optimized[10] binwidth: *global* and *local*
  - Bayesian local adaptive binwidth (BAKS)[11]
- The kernel choice does not matter *that* much[12]
- The estimators based on X_i operate differently – **no pooling**!

[10] Shimazaki, H. & Shinomoto, S. (2010) 'Kernel bandwidth optimization in spike rate estimation', *J. Comput. Neurosci.* 29, 171–182

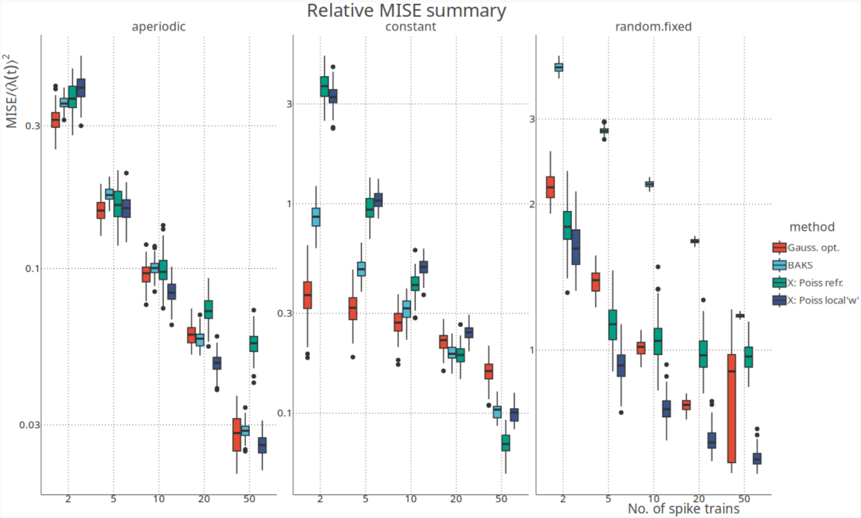
[11] Ahmadi, N., Constandinou, T. G. & Bouganis, C-S. (2018) 'Estimation of neuronal firing rate using Bayesian Adaptive Kernel Smoother (BAKS)', *PLoS ONE* 13, e0206794

[12] Nawrot, M., Aertsen, A. & Rotter, S. (1999) 'Single-trial estimation of neuronal firing rates: from single-neuron spike trains to population activity', *J. Neurosci. Meth.* 94, 81–92

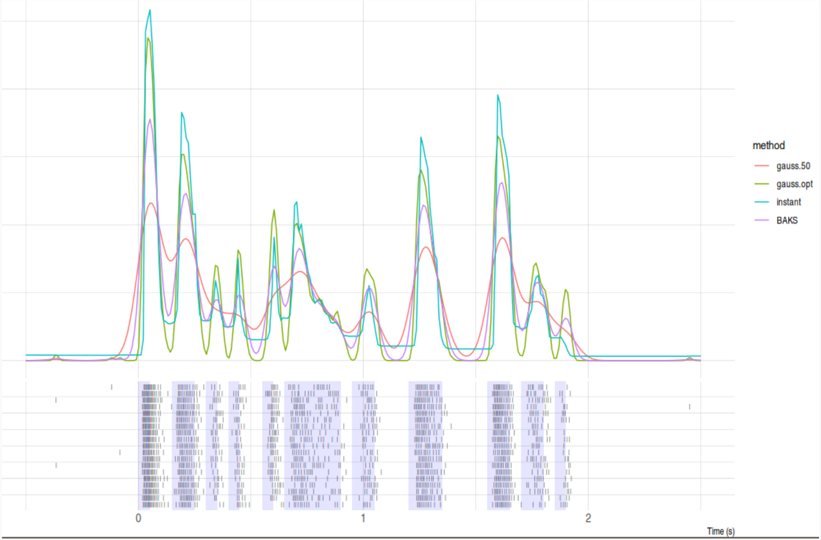
Example: simulated data (Pois, τ_r), rapid switching of $\lambda(t)$



Simulated data: comparison, different $\lambda(t)$ profiles



Example: experimental data (moth ORN) – 'biased' $\widehat{\lambda}_{ML}$



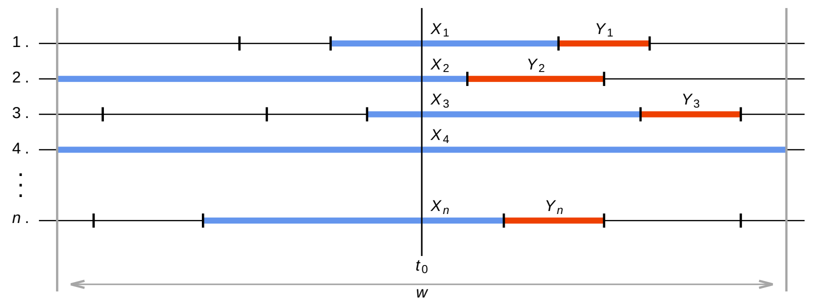
Tentative summary (firing rate estimation from X_i)

- Apparently, there is no single *universally* optimal firing rate estimator under all circumstances
- Standard methods: *pooling* of parallel spike trains
- Estimation based on *instantaneous* ISIs X:
  - Computationally efficient (simple)
  - MLE (and MSE!) can be derived for many cases of interest under the renewal assumption
  - No pooling
  - Non-parametric *vs.* **mismatched** estimation: a *real* problem?
  - Usage for more general situations (non-stationarity)
  - Upward-bias in non-stationary case: different "solutions"?

Estimation of local (instantaneous) spike train variability

Estimation of local spike train variability

- N.B.: assume n parallel spike trains, $\{X_i\}$ realizations of X



- Recall: $X \sim \lambda x f_Y(x), \quad Y \sim f_Y(y) \quad$ and $\lambda = 1/\,\mathrm{E}(Y)$.
- *Local* spike train variability around t_0 (renewal or not).

Fano factor

- The relation between X and Y yields the moment equation:

$$\mathrm{E}(X^k) = \lambda\,\mathrm{E}(Y^{k+1}), \quad k \in \mathbb{Z}$$

- Classical measure of *variability* based on counts (N_i in i-th trial)

$$FF(w) = \frac{\mathrm{Var}[N(t, t+w)]}{\mathrm{E}[N(t, t+w)]} \quad \Rightarrow \widehat{FF}_N = \frac{\sigma^2(N_i)}{\langle N_i \rangle}$$

- *Renewal PP*: often $w \to \infty$ thus[13] $FF = C_V^2 = \mathrm{Var}(Y)/\,\mathrm{E}(Y)^2$
- Therefore:

$$FF = \mathrm{E}\left(\frac{1}{X}\right)\mathrm{E}(X) - 1$$

[13] Cox, D. R. (1962) *Renewal Theory*, London: Methuen and Co. Ltd.

Estimator of *FF* based on instantaneous ISIs

- $\Rightarrow$ estimator (note that $\mathrm{E}(\widehat{FF}_X) = FF$)

$$\widehat{FF}_X = \frac{1}{(n-1)n}\sum_{i=1}^{n}\frac{1}{X_i}\sum_{i=1}^{n}X_i - 1$$

- $\mathrm{Var}(\widehat{FF}_X)$ can be derived[14] in a closed form: contains $\mathrm{E}(1/Y)$
- $\mathrm{E}(1/Y) < \infty$ if[15] f_Y continuous, $f_Y(0) = 0$ and finite $f'_Y(0)$.
- The important role of *refractory period* τ_r!

[14] Rajdl, K. & Kostal, L. (2023) 'Estimation of the instantaneous spike train variability', (submitted)
[15] Piegorsch, W. & Casella, G. (1985) 'The Existence of the First Negative Moment', *Am. Stat.* 39, 60–62

Additional estimators

- "Remove" $\mathrm{E}(1/Y)$: combine X and $N(t - w/2, t + w/2)$:

$$\widehat{FF}_{XN}(w) = \frac{1}{wn^2} \sum_{i=1}^{n} N_i \sum_{i=1}^{n} X_i - 1$$

- $\widehat{FF}_{XN}$ is also unbiased, *curious* case $w_0 = \langle X_i \rangle$:

$$\boxed{\widehat{FF}_{XN}(w_0) \equiv \widehat{FF}_{XN} = \langle \#\text{APs in } w_0 \rangle - 1}$$

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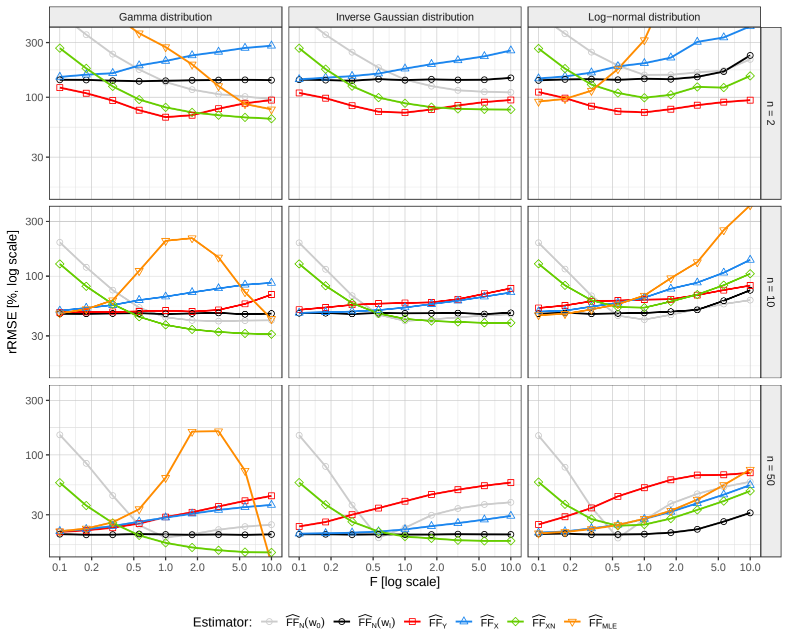
- MLE available for many models of Y (γ, logn, iG: $\widehat{FF}_X$)
- Poisson with $\tau_r > 0$

$$\widehat{FF}_{ML} = \left(\frac{\langle X_i \rangle}{\langle X_i \rangle + 2\min(X_i)}\right)^2$$

- For completeness (C_V^2): $\widehat{FF}_Y$ based on Y_i (not *local* w.r.t. t_0)

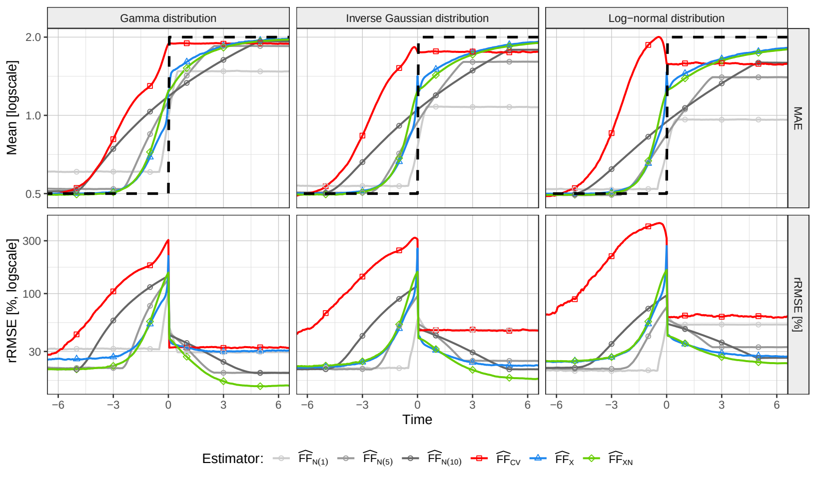
Example results, average values, $\lambda = 1, \tau_r = 0.1$



Estimation of $FF = C_V^2$ under renewal PP

- No *universally optimal* estimator ... **but**:
- Compare $\widehat{FF}_N(w)$ with $\widehat{FF}_{XN}(w)$ at $w = w_0$ or "$w = \infty$"
  - Surprisingly, $\widehat{FF}_N(\infty)$ is rarely optimal (*bias?*)
  - Almost always: $\mathrm{MSE}[\widehat{FF}_N(w_0)] > \mathrm{MSE}[\widehat{FF}_{XN}(w_0)]$
  - (Using *exact* λ in $\widehat{FF}_{XN}$ does not help!)
- MSE of $\widehat{FF}_X$ grows with theoretical FF
- MLE: not as good as expected?
- **Conclusion**: on "average" $\widehat{FF}_{XN}(w_0)$ is the most accurate

Example results: change-point with respect to C_V^2



Estimation of *FF* in "non-stationary" situations

- Change-point[16] with respect to: *variability* vs. *rate*
  - Variability: again, $\widehat{FF}_{XN}$ seems like a good option
    - (Quickly captures the correct *FF* *after* the change point)
  - Rate: "standard" estimators perform better, *however*, we can employ the *operational time*[17]
- Extension to more general non-stationary cases? → combine *firing rate estimation* and *time re-scaling*.

[16] Rajdl, K. & Kostal, L. (2023) 'Estimation of the instantaneous spike train variability', (submitted)
[17] Rajdl, K., Lansky, P. & Kostal, L. (2020) 'Fano factor: a potentially useful information', *Front. Comput. Neurosci.* 14, 569049

Summary

Conclusions

- The key difference between "standard" ISIs Y_i and "instantaneous" ISIs X_i
- The distributions of Y and X differ: length-bias
- If we wish to estimate firing rate (at some time t) then
  - It is *inevitable* to employ X_i
  - Using Y_i is contradictory (spike at time t)
- *Simple* and potentially useful estimators
  - Firing rate
  - Fano factor
  - ...

Thanks to

- Kamil Rajdl, *Petr Lansky*