Detection of Code Juggling with Spike Counts Data Analysis

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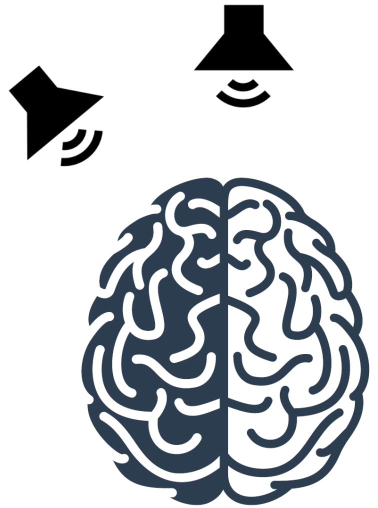
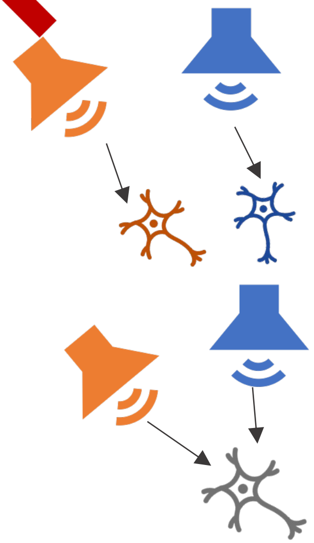
Motivation

How does brain preserve information about multiple simultaneous items ?



- Designated neurons for each signal



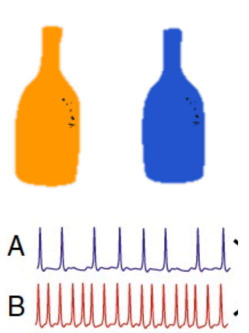
- Small receptive field (perceptual sensitivity)

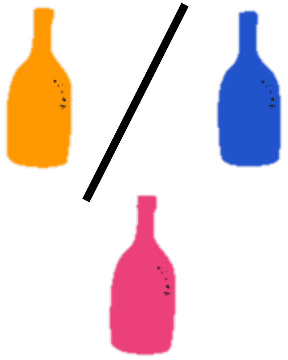
- Receptive fields too large
  - Visual (Alonso and Chen, 2009; Keliris et al., 2019)
  - Auditory (Groh et al., 2003; Werner-Reiss and Groh, 2008; Bulkin and Groh, 2011)

A single neuron will be exposed to multiple simultaneous stimuli !

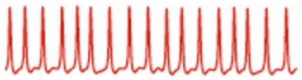
- Dynamics in presentation in a neural level
- Can a single neuron preserve info from both  and 

Motivation: potential dynamics





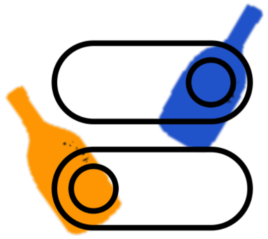
- Always encode A (or B)



- 1st order stochasticity
- Poisson distribution

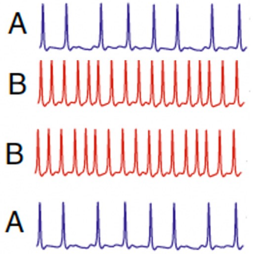
(Ventura et al., 2002; Kass et al., 2005)

- Treat it as a new stimulus

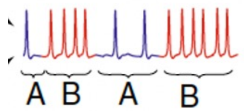


- Switch between A and B
- **Code Juggling**
- **2nd order stochasticity: constituent stimuli**
- Greater efficiency on information preserving
- Overdispersed + bounded by A & B

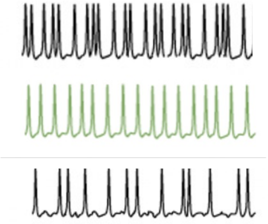
- Across trials
(Caruso et al., 2018)



- Within a trial
(Glynn et al., 2021)



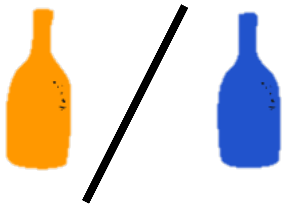
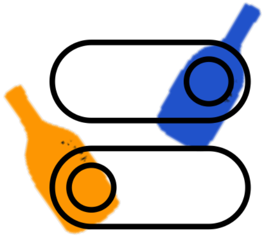
- Stochasticity not related A nor B
- Overdispersed
- Not related to A nor B



Higher trial-to-trial variability
(Semedo et al., 2019)

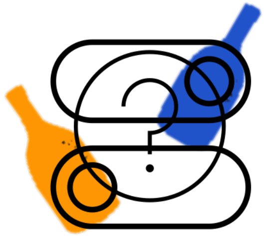
Research question:

How to model these biologically meaningful encoding schemes?

Poisson Mixtures

How to select the most likely scheme and quantify the uncertainty?

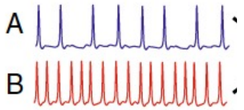


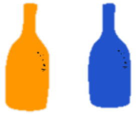
Hypothesis Testing
(Bayes Factor)

Statistical Analysis Framework

Assumptions:

- Two-stimuli cases





- Single stimulus spike counts follow Poisson distribution

$$P^{\mathrm{A}} = \mathrm{Poi}(\mu^{\mathrm{A}}),\ \ P^{\mathrm{B}} = \mathrm{Poi}(\mu^{\mathrm{B}}), \qquad \mu^{\mathrm{A}}, \mu^{\mathrm{B}} > 0.$$

Data: $(Y_j^e : j \in \{1, \ldots, n_e\}, e \in \{\mathrm{A}, \mathrm{B}, \mathrm{AB}\})$

Hypotheses:

$$\text{FIXED: } P^{\mathrm{AB}} = \mathrm{Poi}(\mu), \qquad \mu \in (0, \infty),$$

(whole-trial)

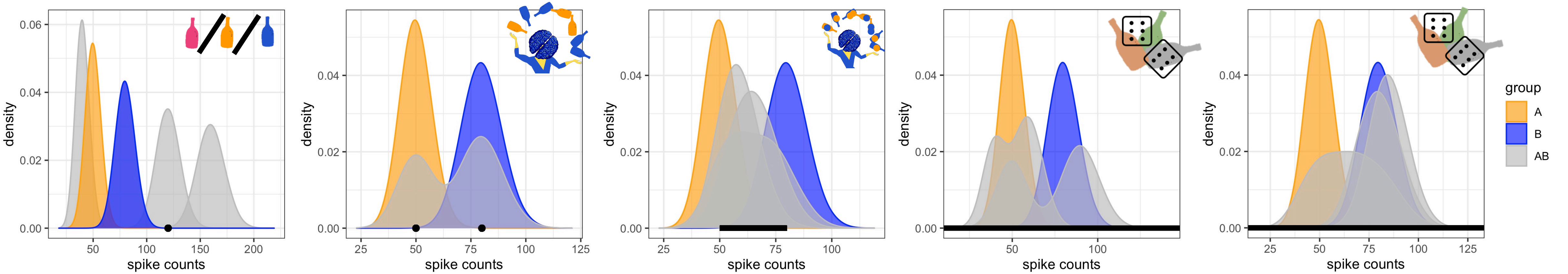
$$\text{MIXTURE: } P^{\mathrm{AB}} = \rho \mathrm{Poi}(\mu^{\mathrm{A}}) + (1-\rho)\mathrm{Poi}(\mu^{\mathrm{B}}), \qquad \rho \in (0,1),$$

(sub-trial)

$$\text{INTERMEDIATE: } P^{\mathrm{AB}} = \int \mathrm{Poi}(r\mu^{\mathrm{A}} + (1-r)\mu^{\mathrm{B}}) f(r) dr, \qquad f \text{ is a density on } (0,1),$$

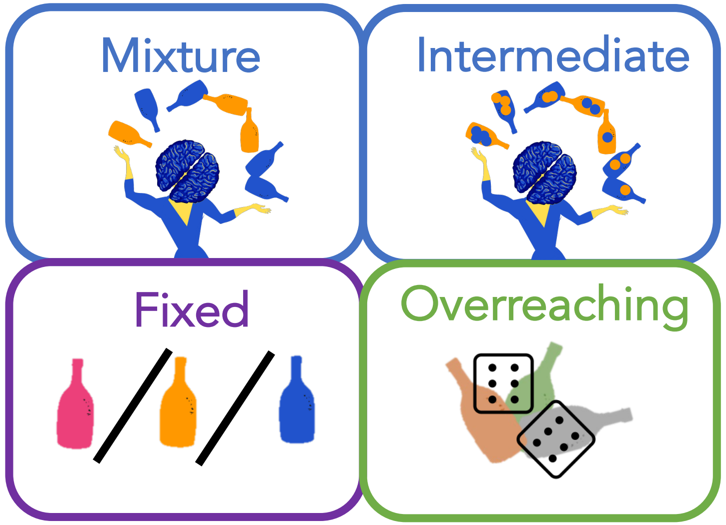
$$\text{OVERREACHING: } P^{\mathrm{AB}} = \int \mathrm{Poi}(m) g(m) dm, \qquad g \text{ is a density on } (0, \infty),$$

Probability distributions (support + continuity):



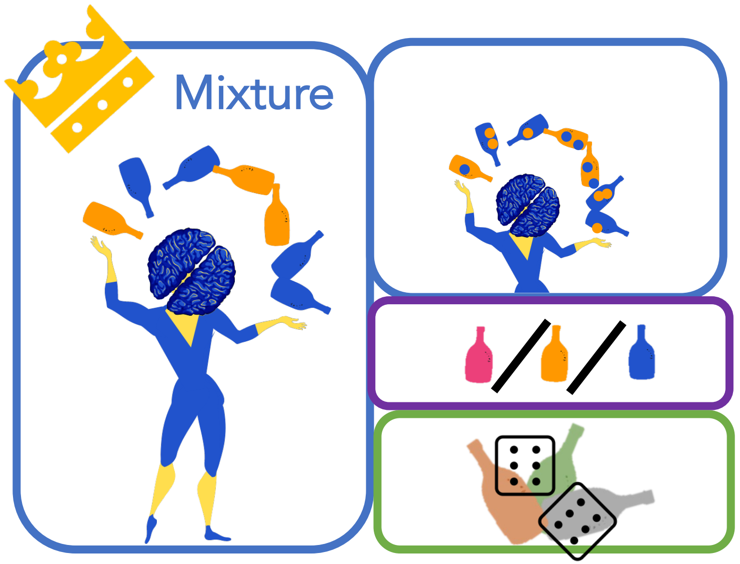
Hypothesis Testing in a Bayesian framework

Prior + Data → Posterior



Spike counts

$$(Y_j^e : j \in \{1, \ldots, n_e\}, e \in \{A, B, AB\})$$



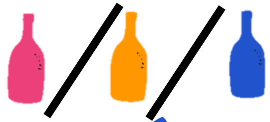
Challenges: nonparametric density estimation and fair competition

Predictive recursion marginal likelihood method (PRML)

(Newton et al., 1998; Newton, 2002; Tokdar et al., 2009; Martin and Tokdar, 2011)

Statistical Analysis Framework

Hypotheses:



FIXED: $P^{AB} = \mathrm{Poi}(\mu), \quad \mu \in (0, \infty),$

MIXTURE: $P^{AB} = \rho \mathrm{Poi}(\mu^{A}) + (1-\rho)\mathrm{Poi}(\mu^{B}), \quad \rho \in (0,1),$

INTERMEDIATE: $P^{AB} = \int \mathrm{Poi}(r\mu^{A} + (1-r)\mu^{B}) f(r)dr, \quad f$ is a density on $(0,1)$,

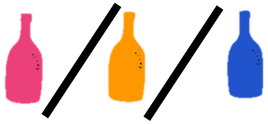
OVERREACHING: $P^{AB} = \int \mathrm{Poi}(m)g(m)dm, \quad g$ is a density on $(0,\infty)$,

Straightforward

unknown

unknown

Statistical Analysis Framework

Hypotheses:  FIXED: $P^{\mathrm{AB}} = \mathrm{Poi}(\mu),$ $\mu \in (0, \infty),$

Marginal likelihood: $p(Y^{\mathrm{A}}, Y^{\mathrm{B}}, Y^{\mathrm{AB}}) = \cancel{p(Y^{\mathrm{A}})p(Y^{\mathrm{B}})}\,p(Y^{\mathrm{AB}} | Y^{\mathrm{A}}, Y^{\mathrm{B}})$

$$p(Y^{\mathrm{AB}} | Y^{\mathrm{A}}, Y^{\mathrm{B}}) = p(Y^{\mathrm{AB}}) = \int p(Y^{\mathrm{AB}} | \mu) \pi(\mu) d\mu$$

Set a prior and can obtain closed form

Statistical Analysis Framework

OVERREACHING: $P^{AB} = \int \text{Poi}(m) g(m) dm,$ g is a density on $(0, \infty)$,

Marginal likelihood: $p(Y^{AB} | Y^{A}, Y^{B}) = p(Y^{AB})$

Predictive Recursion (Smith and Markov, 1978; Newton et al., 1998; Newton, 2002)

Data $Y_1, \ldots, Y_n$ from mixture distribution

known unknown

$$m_f(y) = \int \kappa(y \mid u) f(u) d\nu(u)$$

For $i \in \{1, \ldots, n\}$

$$f_i(u) = (1 - w_i) f_{i-1}(u) + w_i \frac{\kappa(Y_i \mid u) f_{i-1}(u)}{m_{i-1}(Y_i)}, \; u \in \mathcal{U},$$

$$m_{i-1}(y) = \int \kappa(y \mid u) f_{i-1}(u) d\nu(u), \quad y \in \mathcal{Y}$$

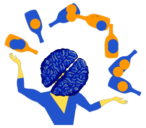
Theoretical guarantee (Tokdar et al., 2009) :

f_n m_n converge to the truth asymptotically (provided $\sum_{i=1}^{\infty} w_i = \infty$ $\sum_{i=1}^{\infty} w_i^2 < \infty$)

Bayesian inferential paradigm interpretation (Tokdar et al., 2009)

Statistical Analysis Framework

$$\text{MIXTURE: } P^{\mathrm{AB}} = \rho \mathrm{Poi}(\mu^{\mathrm{A}}) + (1-\rho)\mathrm{Poi}(\mu^{\mathrm{B}}), \qquad \rho \in (0,1),$$



$$\text{INTERMEDIATE: } P^{\mathrm{AB}} = \int \mathrm{Poi}(r\mu^{\mathrm{A}} + (1-r)\mu^{\mathrm{B}}) f(r) dr, \qquad f \text{ is a density on } (0,1),$$

Marginal likelihood:

$$p(Y^{\mathrm{AB}} | Y^{\mathrm{A}}, Y^{\mathrm{B}}) = \int p(Y^{\mathrm{AB}} | \theta) p(\theta | Y^{\mathrm{A}}, Y^{\mathrm{B}}) d\theta \qquad \theta = (\mu^{\mathrm{A}}, \mu^{\mathrm{B}})$$

First-stage prior:

$$\pi_0(\mu^{\mathrm{A}}, \mu^{\mathrm{B}}) = 1/\sqrt{\mu^A \mu^{\mathrm{B}}},$$

Second-stage prior:

$$\pi(\mu^{\mathrm{A}}, \mu^{\mathrm{B}}) = \mathrm{Gam}(\mu^{\mathrm{A}} \mid 0.5 + \textstyle\sum_{j=1}^{n_{\mathrm{A}}} Y_j^{\mathrm{A}}, n_{\mathrm{A}}) \times \mathrm{Gam}(\mu^{\mathrm{B}} \mid 0.5 + \textstyle\sum_{j=1}^{n_{\mathrm{B}}} Y_j^{\mathrm{B}}, n_{\mathrm{B}})$$

$$m_f(y) = \int \kappa_\theta(y \mid u) f(u) d\nu(u)$$

PRML score

(Martin and Tokdar, 2011)

Predictive Recursion Marginal Likelihood

Data $Y_1, \ldots, Y_n$ from mixture distribution

$i \in \{1, \ldots, n\}$

Predictive Recursion

(Newton et al., 1998; Newton, 2002)

$$m_f(y) = \int \kappa_\theta(y \mid u) f(u) d\nu(u)$$

$$f_i(u) = (1 - w_i) f_{i-1}(u) + w_i \frac{\kappa_\theta(Y_i \mid u) f_{i-1}(u)}{m_{i-1}(Y_i)}, \; u \in \mathcal{U},$$

$$m_{i-1,\theta}(y) = \int \kappa_\theta(y \mid u) f_{i-1}(u) d\nu(u), \quad y \in \mathcal{Y}$$

$\kappa = \kappa_\theta$

PRML score

(Martin and Tokdar, 2011)

$$L_n(\theta) := \prod_{i=1}^{n} m_{i-1,\theta}(Y_i)$$

- PRML score estimate true marginal density: $p(Y_1, \ldots, Y_n \mid \theta) = \prod_{i=1}^{n} p(Y_i \mid Y_1, \ldots, Y_{i-1}, \theta)$
- Asymptotic consistency: $n^{-1} \log\{L_n(\theta)/L_n(\theta^\star)\} \to -\inf_{f \in \mathbb{F}} d_{\mathrm{KL}}(m^\star, m_{f,\theta})$.
- Interpretable: expectation filtration approximation to a fully Bayesian estimation $w_i = (1 + a)^{-1}, \; a > 0$

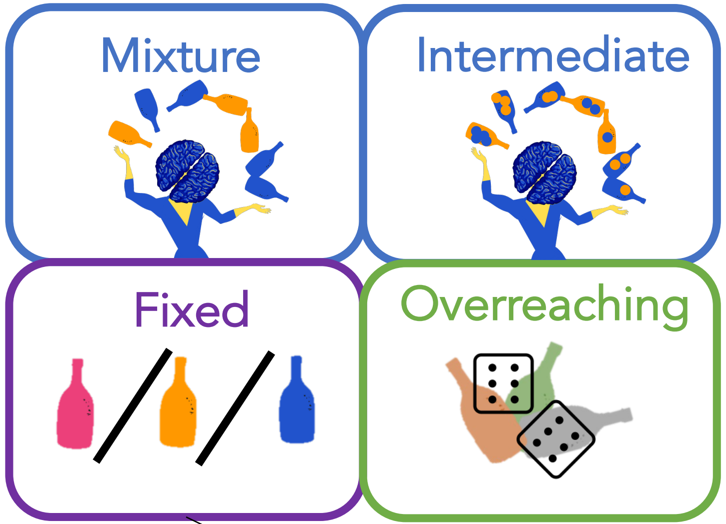
Laplace Approximation:

$$I(M_h) := \int_{\Theta_h} L_{n,h}(\theta_h) \pi_h(\theta_h) d\theta_h, \quad h \in H,$$

$$\hat{I}(M_h) = L_{n,h}(\hat{\theta}_h)(2\pi)^{-d_h/2} |\Sigma_h|^{1/2},$$

Fair competition: choice of prior

Prior + Data → Posterior



Spike counts

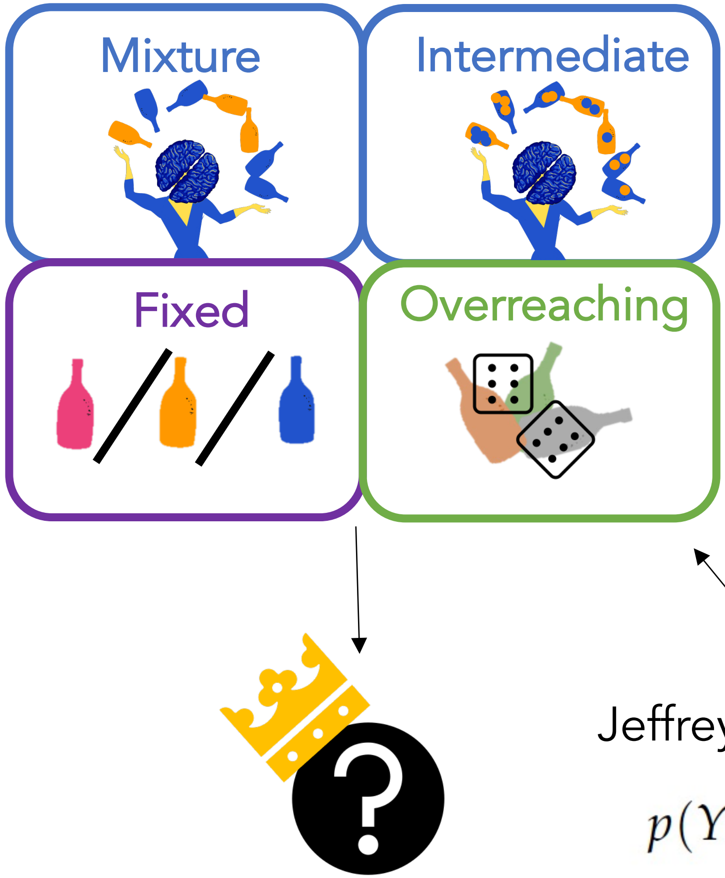
$$(Y_j^e : j \in \{1, \ldots, n_e\}, e \in \{\mathrm{A}, \mathrm{B}, \mathrm{AB}\})$$

$$p_h(Y) = \frac{I(M_h)\, p_{0,h}}{\sum_{h' \in H} I(M_{h'})\, p_{0,h'}}$$

- Sensitive to the choice of prior
  - Bounded uniform (same as overreaching)
  - Jeffreys' prior (improper) - - > tune the constant
  - Jeffreys' prior (intrinsic Bayes factor) (Berger & Pericchi, 1996)

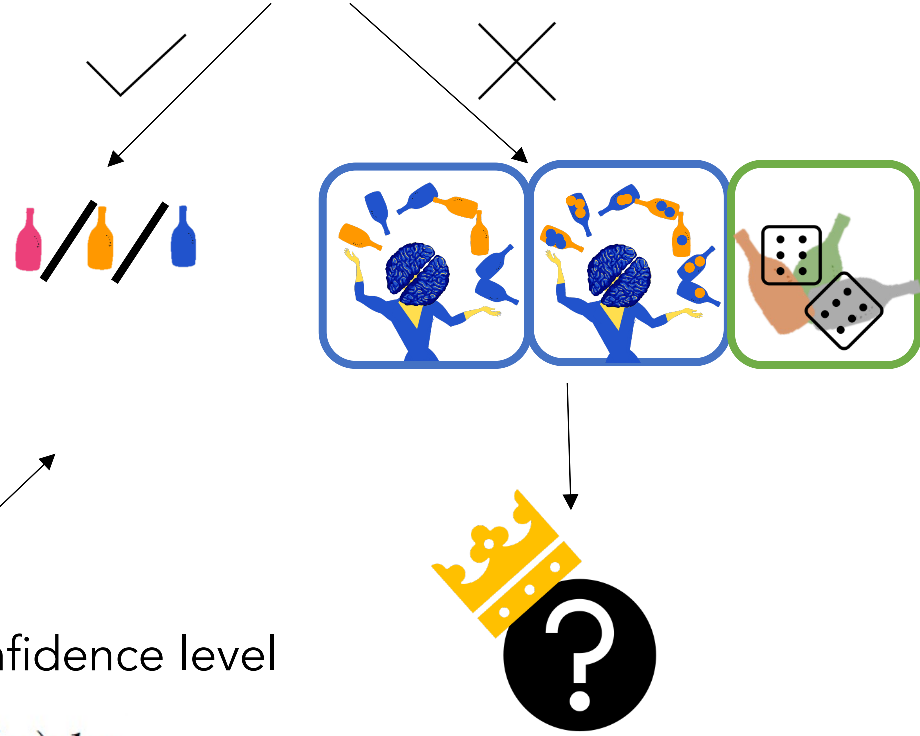
Two potential frameworks

Full Bayesian



Two-stage procedure

Poisson variance test → Is it Fixed?
(Brown and Zhao, 2002)



Jeffreys’ prior: tune constant to match the confidence level

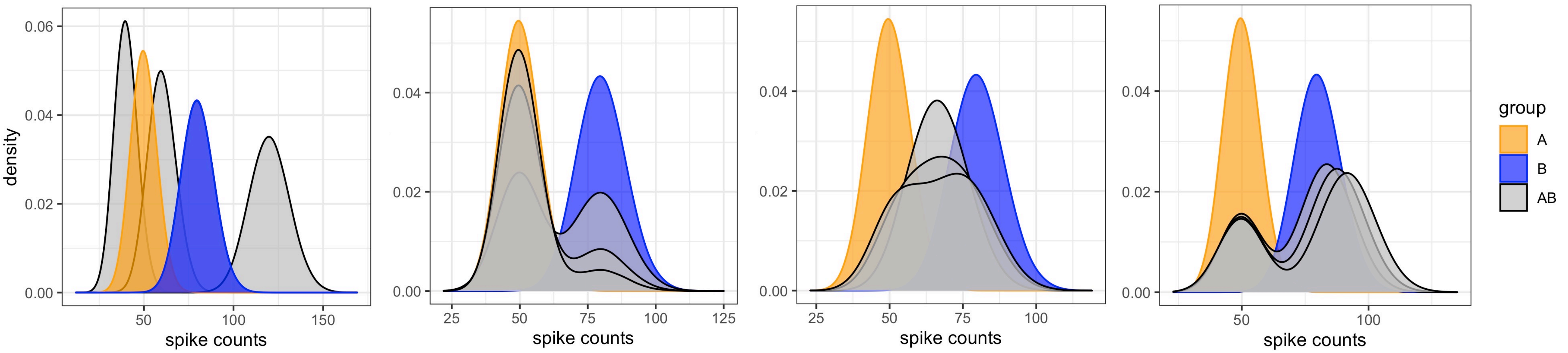
$$p(Y^{\mathrm{AB}}|Y^{\mathrm{A}}, Y^{\mathrm{B}}) = p(Y^{\mathrm{AB}}) = \int p(Y^{\mathrm{AB}}|\mu)\pi(\mu)d\mu$$

$$\pi(\mu) \propto \mu^{-1/2}$$

Performance Assessment

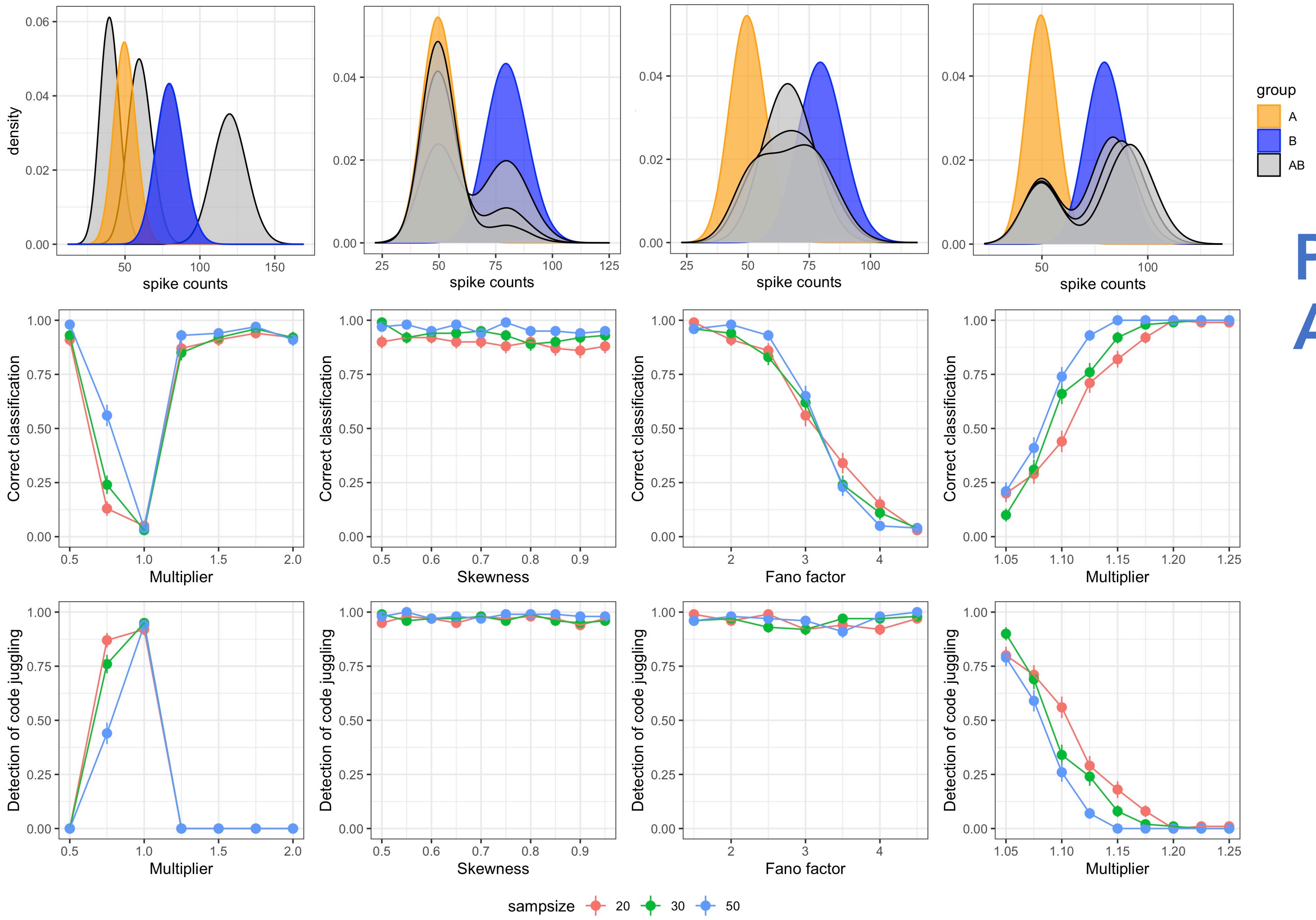
100 experiment sets: $P^{A} = \text{Poi}(50)$ $P^{B} = \text{Poi}(80)$ $n_A = n_B = n_{AB}$

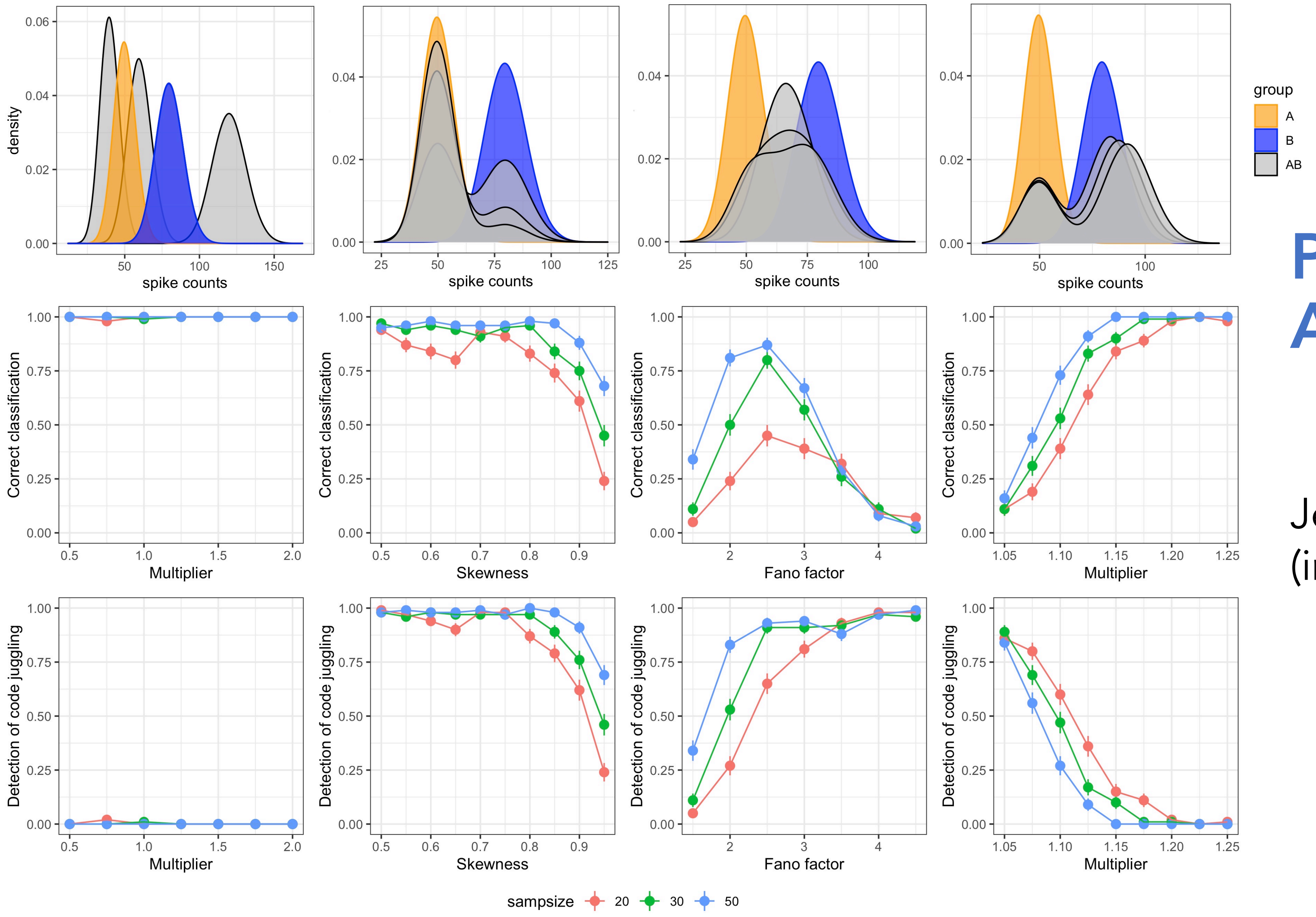
FIXED:	$P^{AB} = \text{Poi}(80m)$	Multiplier
MIXTURE:	$P^{AB} = m\text{Poi}(50) + (1-m)\text{Poi}(80)$	Skewness
INTERMEDIATE:	$P^{AB} = \int \text{Poi}(r50 + (1-r)80)\text{Beta}(r; a, b)dr$	Fano factor
OVERREACHING:	$P^{AB} = 1/3\text{Poi}(50) + 2/3\text{Poi}(80m)$	Multiplier



Performance Assessment

Bounded Uniform



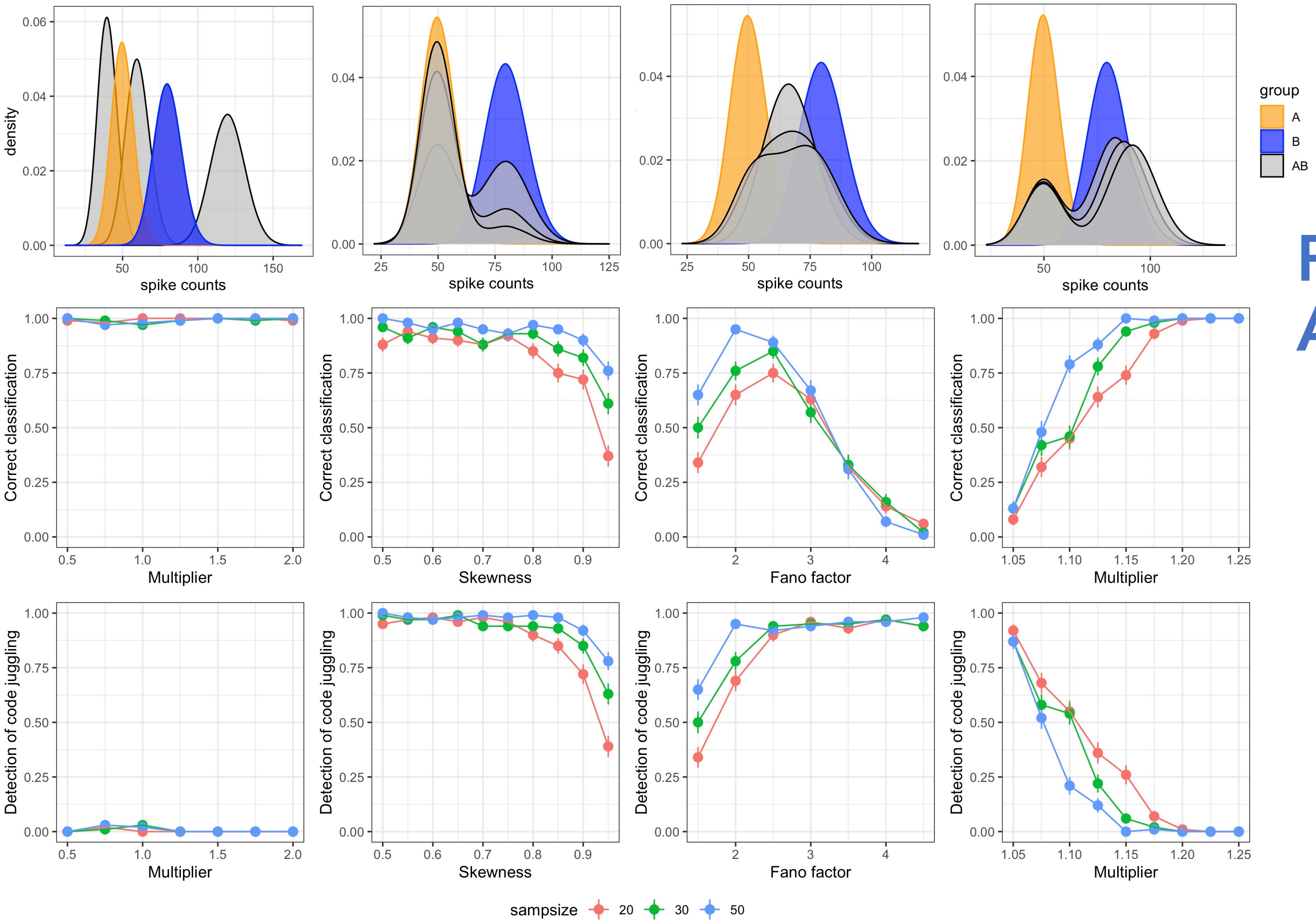


Performance Assessment

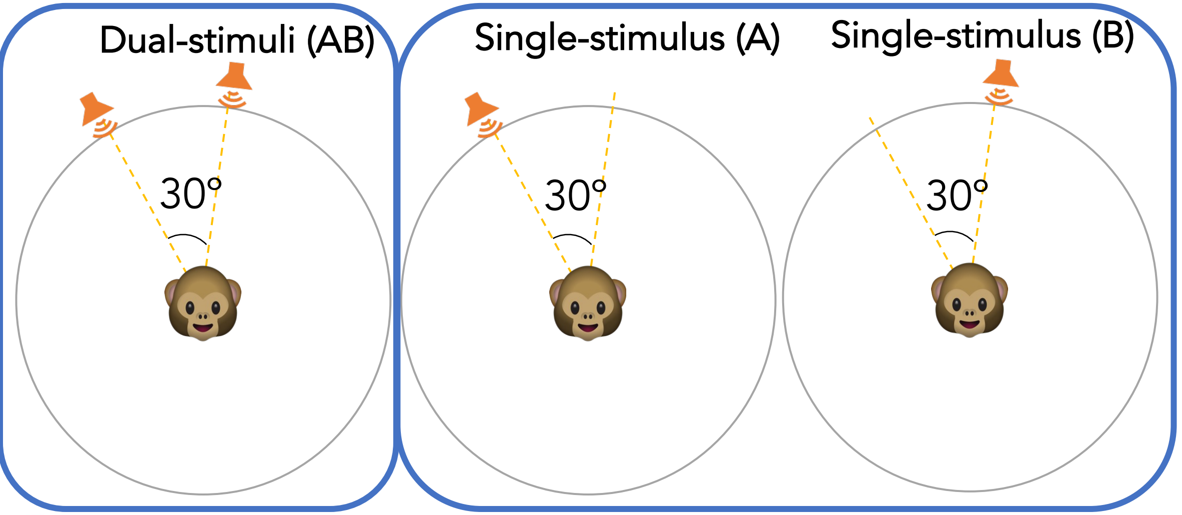
Jeffreys’ prior
(intrinsic Bayes factor)

Performance Assessment

Jeffreys' prior (w/ constant 1)



Application in IC data

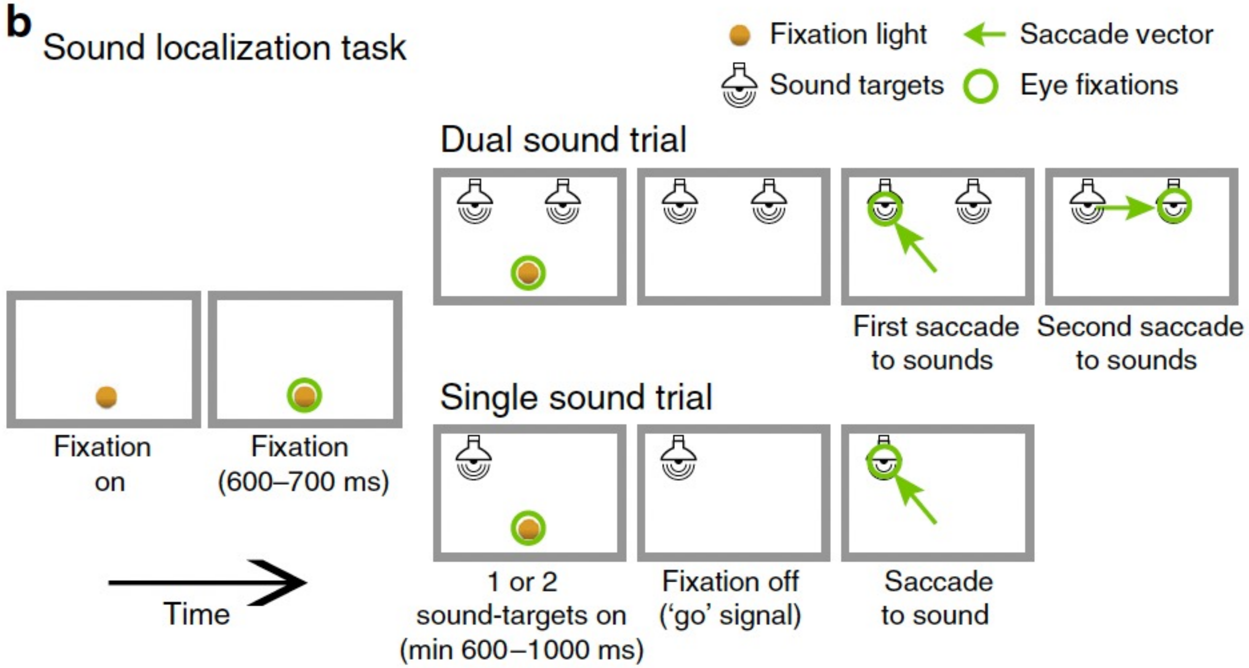


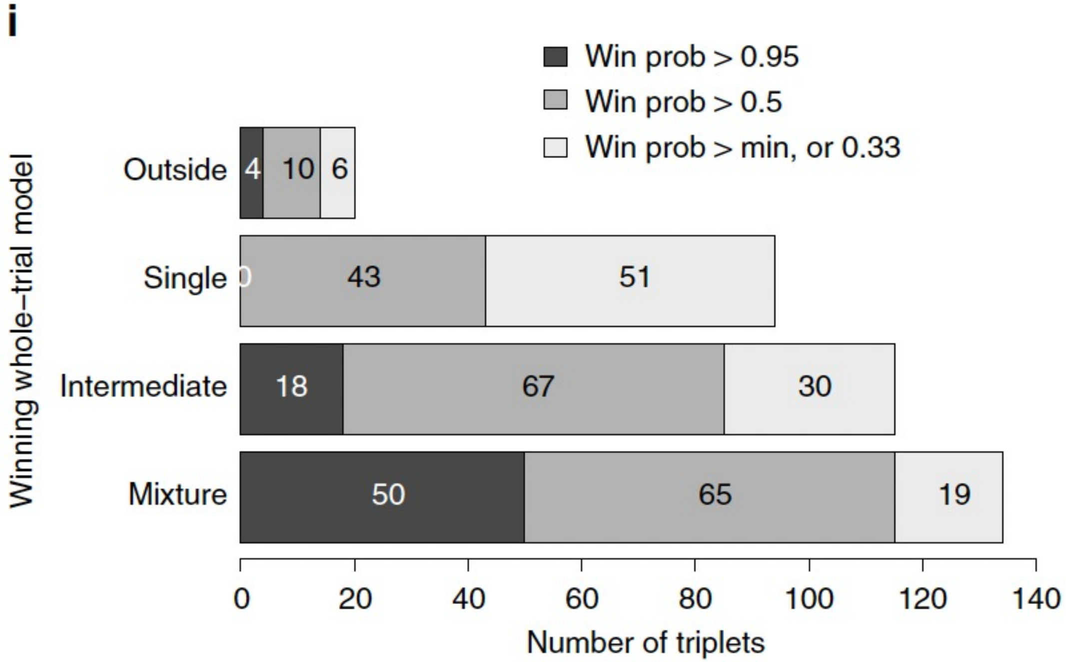
Experiment design (Caruso et al., 2018)

- Localization task: eye movements to sound (saccades)
- Single cell recording in Inferior colliculus (IC): accurate sound localization

Results from Caruso et al. (2018)

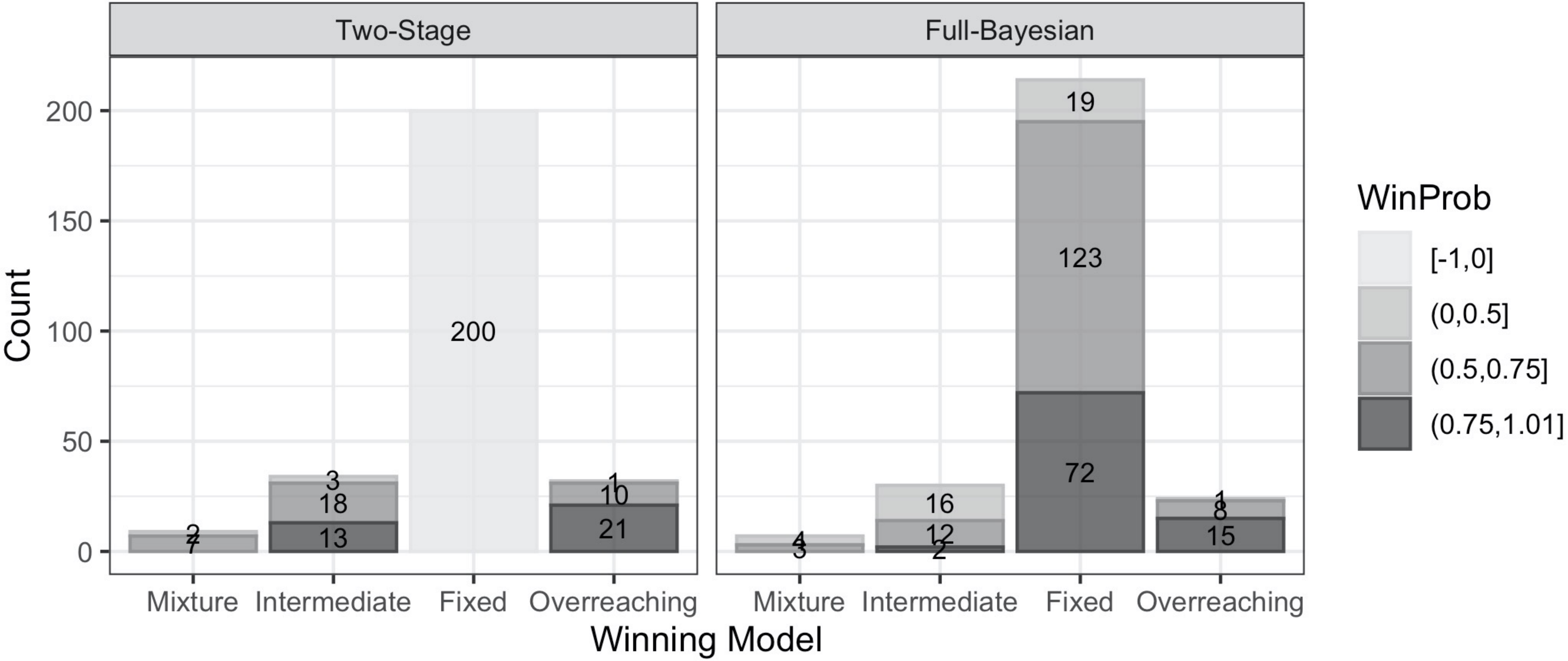
- Chi-square goodness of fit test: 363 triplets



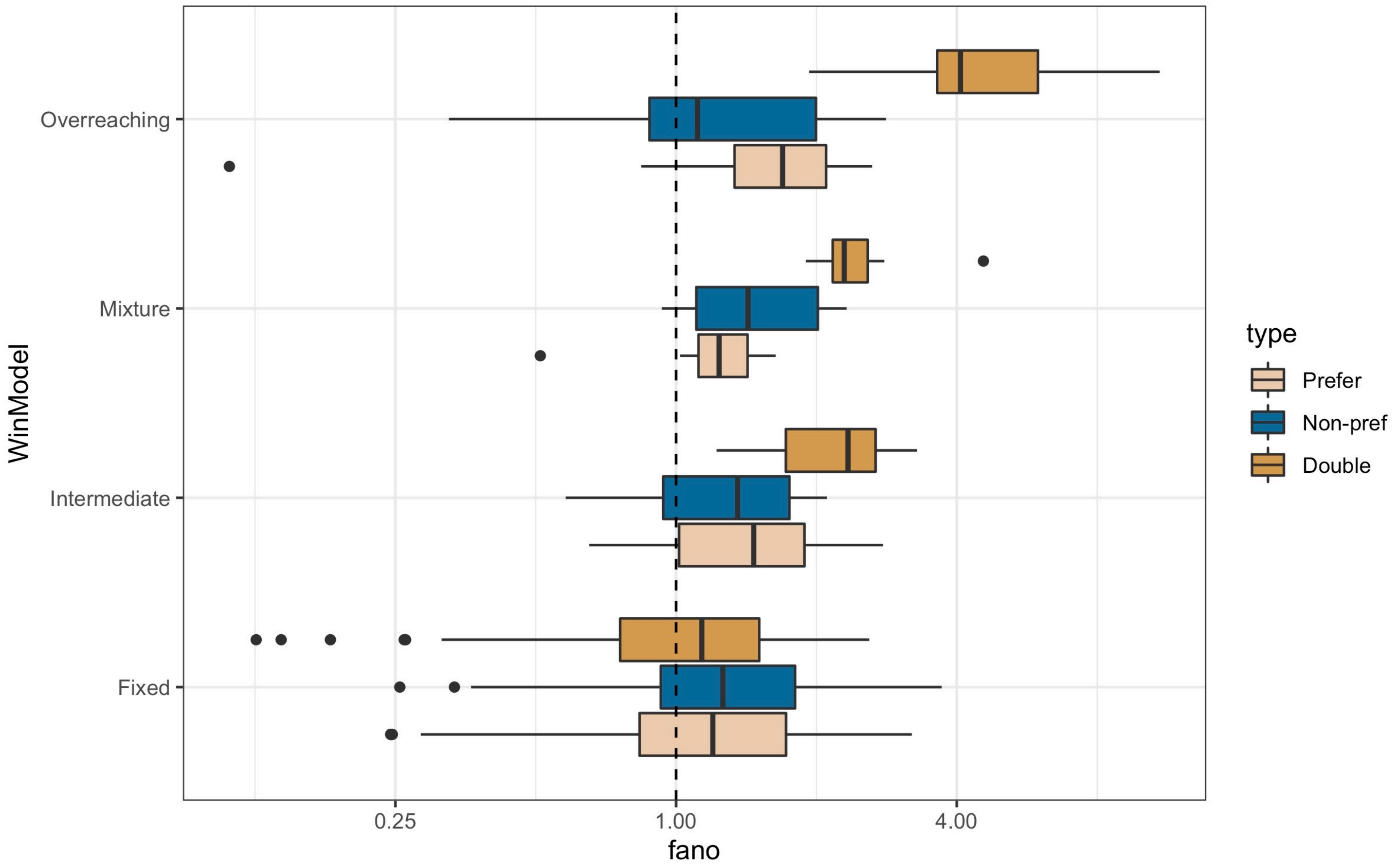


Results

Preprocessing: Poisson variance test (Brown and Zhao, 2002) ensure Poisson-like distribution for single stimulus

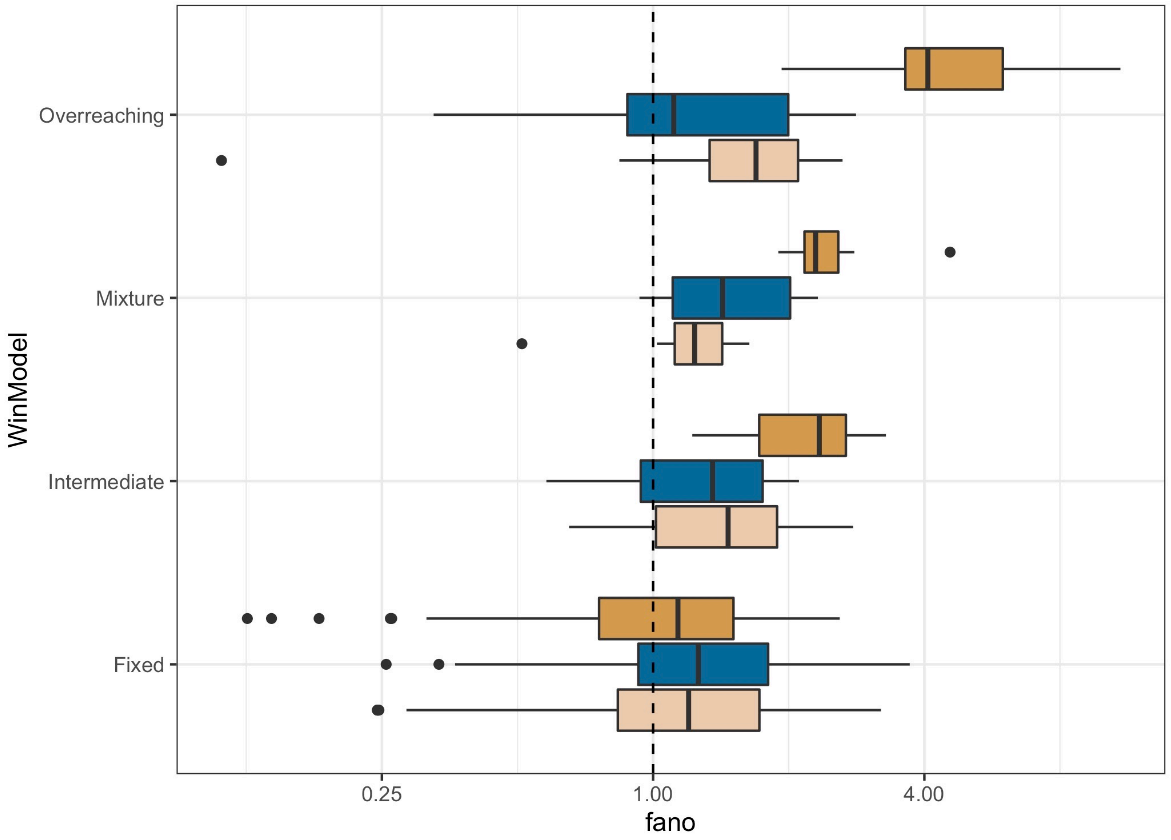


Results

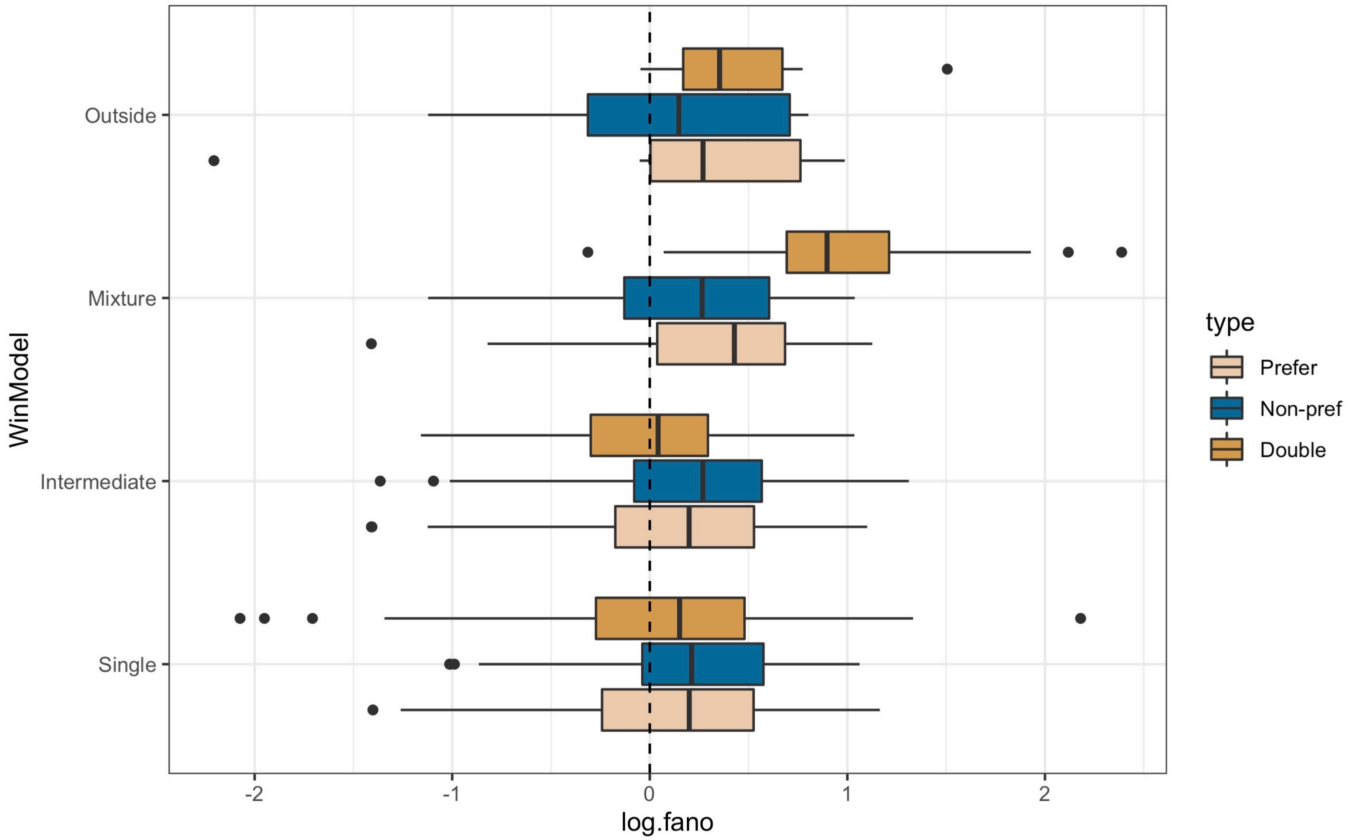

Overreaching
Mixture
Intermediate
Fixed
WinModel
0.25
1.00
4.00
fano
type
Prefer
Non-pref
Double

Results

New Method



Old Poisson



Thank you

Reference

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PRML Algorithm

Input: i.i.d observations $Y_1, ..., Y_n$
Output: marginal likelihood $L_n(\theta) = \prod_{i=1}^n m_{i-1,\theta}(Y_i)$, gradient $\nabla \log L_n(\theta) = \sum_{i=1}^n \nabla \log m_{i-1,\theta}(Y_i)$ and mixing density $f_{n,\theta}$
Initialize: $f_{0,\theta} \in \mathbb{F}$ of f (usually uniform);compute $\nabla f_{0,\theta}(u)$;
weights $w_1, .., w_n \in (0,1)$ (usually $w_i = (i+1)^{-\gamma}$)
for $i = 1,...,n$ **do**

$$m_{i-1,\theta}(Y_i) = \int p(Y_i|\theta,u') f_{i-1,\theta}(u') d\mu(u') \tag{13}$$

$$f_{i,\theta}(u) = (1-w_i) f_{i-1,\theta}(u) + w_i \frac{p(Y_i|\theta,u) f_{i-1,\theta}(u)}{m_{i-1,\theta}(Y_i)} \tag{14}$$

For $\nabla f_{i,\theta}(u)$:

$$G(\theta,u) = p(Y_i|\theta,u) \nabla f_{i-1,\theta}(u) + \nabla p(Y_i|\theta,u) f_{i-1,\theta}(u) \tag{15}$$

$$\nabla \log m_{i-1,\theta}(Y_i) = \frac{\int G(\theta,u) d\mu(u)}{m_{i-1,\theta}(Y_i)} \tag{16}$$

$$\nabla f_{i,\theta}(u) = (1-w_i) \nabla f_{i-1,\theta}(u) + w_i \{ \frac{G(\theta,u) - p(Y_i|\theta,u) f_{i-1,\theta}(u) \nabla \log m_{i-1,\theta}(Y_i)}{m_{i-1,\theta}(Y_i)} \} \tag{17}$$

end