Parameter estimation in diffusion processes from observations of first hitting-times

Susanne Ditlevsen
Department of Mathematical Sciences
University of Copenhagen, Denmark
Email: susanne@math.ku.dk

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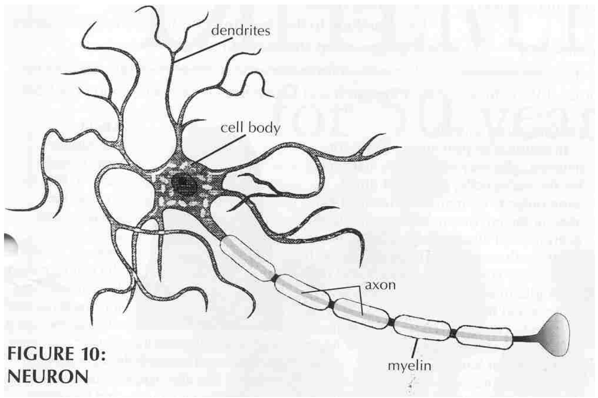
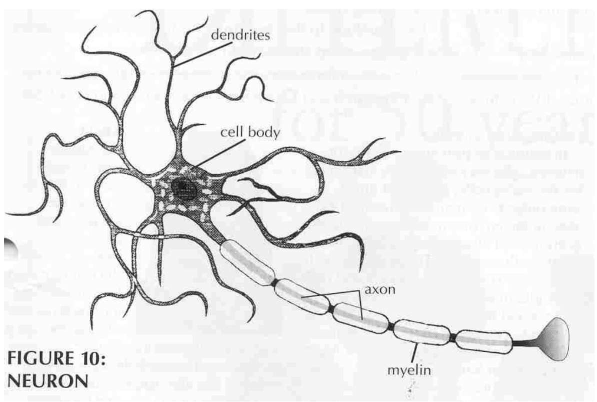
Motivating example: Neurons (nerve cells)

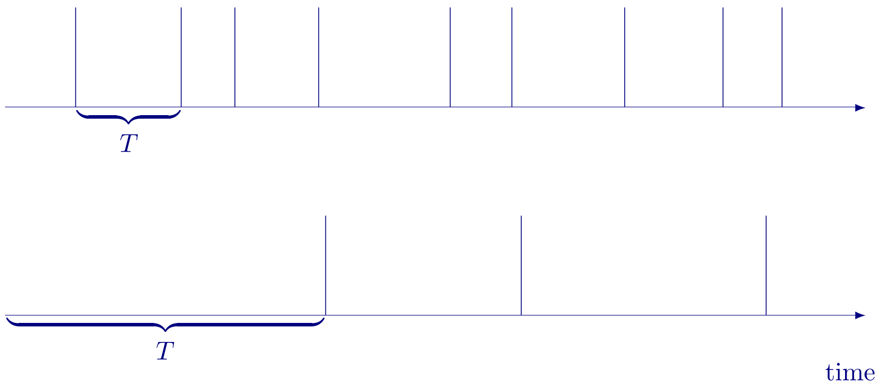


Motivating example: Neurons (nerve cells)

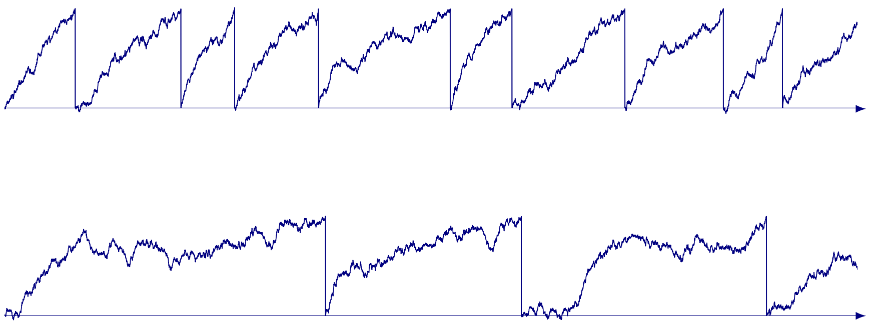


$\Longrightarrow$ •

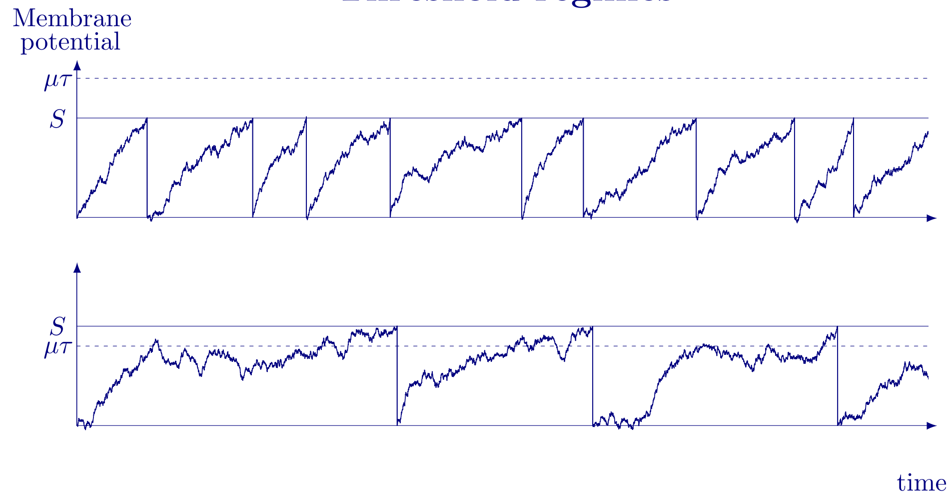
Data: spiketrains



Underlying process



Threshold regimes



The model

$$\mathrm{d}X_t = \mu(X_t)\,\mathrm{d}t + \sigma(X_t)\,\mathrm{d}W(t)\ ;\ X_0 = x_0$$

X_t: membrane potential at time t after a spike

x_0: initial voltage (the reset value following a spike)

An action potential (a spike) is produced when the membrane voltage X_t exceeds a *firing threshold*

$$S(t) = S \quad > \quad X(0) = x_0$$

After firing the process is reset to x_0. The interspike interval T is identified with the first-passage time of the threshold,

$$T = \inf\{t > 0 : X_t \geq S\}.$$

Data

We observe the spikes: the first-passage-time of X_t through S:

Data: $\{t_1, t_2, \ldots, t_n\}$ i.i.d. realizations of the random variable T.

Note: There is only information on the time scale, nothing on the scale of X_t. Thus, obviously something is not identifiable in the model from these data, and something has to be assumed known.

Estimation

$$\mathrm{d}X_t = \mu(X_t, \theta)\,\mathrm{d}t + \sigma(X_t, \theta)\,\mathrm{d}W(t) \quad ; \quad \theta \in \Theta \subseteq \mathbb{R}^p$$

Transition density: $y \mapsto f_\theta(t-s, x, y)$

Corresponding distribution function: $F_\theta(t-s, x, y) = \int^y f_\theta(t-s, x, u)du$

$$T = \inf\{t > 0 : X_t \geq S\}.$$

Data: $\{t_1, t_2, \ldots, t_n\}$ i.i.d. realizations of the random variable T.

How do we estimate θ?

Maximum likelihood estimation

... is possible if we know the distribution of T.

Let $p_\theta(t)$ be the probability density function of T.

Recall:

Likelihood function:	$L_n(\theta)$	$=$	$\prod_{i=1}^n p_\theta(t_i)$
Log-likelihood function:	$\log L_n(\theta)$	$=$	$\sum_{i=1}^n \log p_\theta(t_i)$
Score function(s):	$\partial_\theta \log L_n(\theta)$	$=$	$\sum_{i=1}^n \partial_\theta \log p_\theta(t_i)$
Estimator $\hat\theta$ is such that	$\partial_\theta \log L_n(\hat\theta)$	$=$	0

Example: Brownian motion with drift

$$\mathrm{d}X_t = \mu\,\mathrm{d}t + \sigma\,\mathrm{d}W(t) \quad ; \quad \mu > 0, \sigma > 0 \quad ; \quad X_0 = 0 < S$$

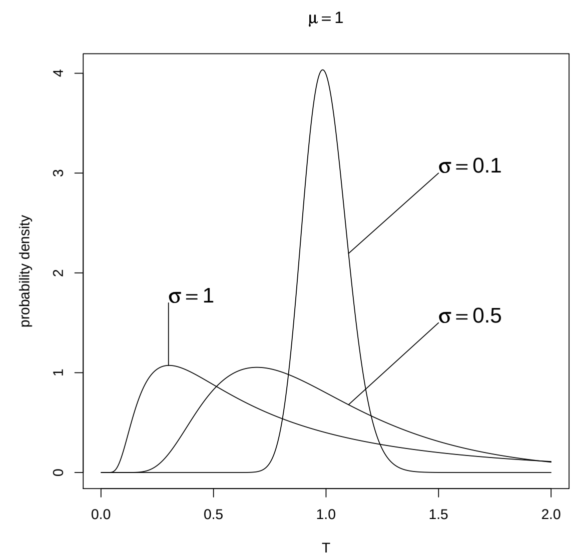
Then

$$p_\theta(t) \;=\; \frac{S}{\sqrt{2\pi\sigma^2 t^3}} \exp\left(-\frac{(S-\mu t)^2}{2\sigma^2 t}\right)$$

Thus

$$L_n(\theta) = \prod_{i=1}^n p_\theta(t_i) \;=\; \prod_{i=1}^n \left(\frac{S}{\sqrt{2\pi\sigma^2 t_i^3}}\right) \exp\left(-\sum_{i=1}^n \frac{(S-\mu t_i)^2}{2\sigma^2 t_i}\right)$$

$$\log L_n(\theta) = \sum_{i=1}^n \log p_\theta(t_i) \;=\; \sum_{i=1}^n \log\left(\frac{S}{\sqrt{2\pi\sigma^2 t_i^3}}\right) - \sum_{i=1}^n \frac{(S-\mu t_i)^2}{2\sigma^2 t_i}$$



Score functions:

$$\partial_\mu \log L_n(\theta) = \sum_{i=1}^{n} \frac{(S-\mu t_i)}{\sigma^2}$$

$$\partial_{\sigma^2} \log L_n(\theta) = -\frac{n}{2\sigma^2} + \sum_{i=1}^{n} \frac{(S-\mu t_i)^2}{2(\sigma^2)^2 t_i}$$

Maximum likelihood estimators:

$$\hat{\mu} = \frac{S}{\bar{t}}$$

$$\hat{\sigma}^2 = S^2 \left(\frac{1}{n} \sum_{i=1}^{n} \frac{1}{t_i} - \frac{1}{\bar{t}} \right)$$

where

$$\bar{t} = \frac{1}{n} \sum_{i=1}^{n} t_i$$

Example: The Ornstein-Uhlenbeck model

Consider the Ornstein-Uhlenbeck process as a model for the membrane potential of a neuron:

$$\mathrm{d}X_t = \left(-\frac{X_t}{\tau} + \mu \right) \mathrm{d}t + \sigma \, \mathrm{d}W_t \;\; ; \;\; X_0 = x_0 = 0.$$

where

X_t: membrane potential at time t after a spike

τ: membrane time constant, reflects spontaneous voltage decay (>0)

μ: characterizes constant neuronal input

σ: characterizes erratic neuronal input

x_0: initial voltage (the reset value following a spike)

The conditional expectation is

$$E[X_t | X_0 = 0] = \mu\tau(1 - e^{-t/\tau})$$

The conditional variance is

$$\mathrm{Var}[X_t | X_0 = x_0] = \frac{\tau\sigma^2}{2} \left(1 - e^{-2t/\tau} \right)$$

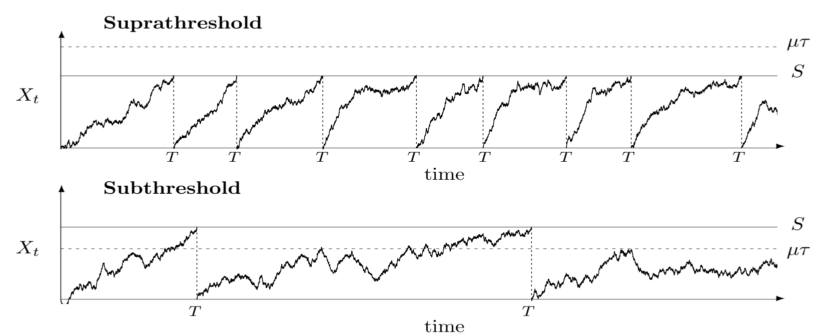
Thus $(X_t | X_0 = 0) \sim N(\mu\tau(1 - e^{-t/\tau}), \frac{\tau\sigma^2}{2} \left(1 - e^{-2t/\tau}\right))$.

Asymptotically (in absence of a threshold) $X_t \sim N(\mu\tau, \tau\sigma^2/2)$.

Two firing regimes:

Suprathreshold: $\mu\tau \gg S$ (deterministic firing - the neuron is active also in the absence of noise)

Subthreshold: $\mu\tau \ll S$ (firing is caused only by random fluctuations (stochastic or Poissonian firing)



Model parameters: $\mu, \sigma, \tau, x_0, S$

Assumed known:

Intrinsic or characteristic parameters of the neuron: τ, x_0, S

$$\tau \approx 5 - 50 \text{ msec}, S - x_0 \approx 10 \text{ mV} \text{ ; (We set } x_0 = 0)$$

To be estimated:

Input parameters: μ (in [mV/msec]) and σ (in [mV/$\sqrt{\text{msec}}$])

Example: Ornstein-Uhlenbeck process

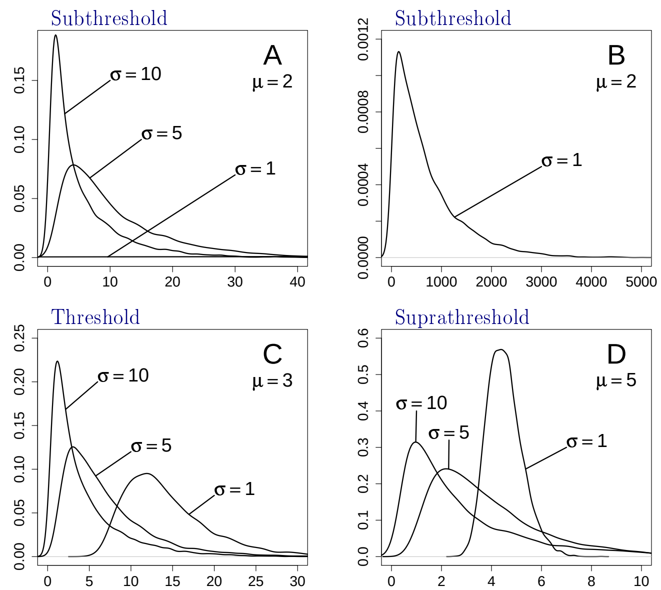
$$\mathrm{d}X_t = \left(-\frac{X_t}{\tau} + \mu\right)\mathrm{d}t + \sigma\,\mathrm{d}W(t)\,;\; \tau > 0, \mu \in \mathbb{R}, \sigma > 0\,;\; X_0 = 0 < S$$

The distribution of $T = \inf\{t > 0 : X_t \geq S\}$ is only known if $S = \mu\tau$ (the asymptotic mean of X_t in absence of a threshold):

$$p_\theta(t) \;=\; \frac{2S\exp(2t/\tau)}{\sqrt{\pi\tau^3\sigma^2}(\exp(2t/\tau)-1)^{3/2}}\exp\left(-\frac{S^2}{\sigma^2\tau(\exp(2t/\tau)-1)}\right)$$

Maximum likelihood estimator ($\mu = S/\tau$ by assumption):

$$\hat{\sigma}^2 \;=\; \frac{1}{n}\sum_{i=1}^{n}\frac{2S^2}{\tau(\exp(2t_i/\tau)-1)}$$



Interspike intervals (ms)

We reformulate to the equivalent dimensionless form

$$\mathrm{d}\Big(\frac{X_t}{S}\Big) = \Big(-\frac{X_t}{S} + \frac{\mu\tau}{S}\Big)\,\mathrm{d}\Big(\frac{t}{\tau}\Big) + \frac{\sigma\sqrt{\tau}}{S}\,\mathrm{d}\Big(\frac{W_t}{\sqrt{\tau}}\Big)$$

or

$$\mathrm{d}Y_s = (-Y_s + \alpha)\,\mathrm{d}s + \beta\,\mathrm{d}W_s, \qquad Y_0 = 0$$

where

$$s = \frac{t}{\tau},\; Y_s = \frac{X_t}{S},\; W_s = \frac{W_t}{\sqrt{\tau}},\; \alpha = \frac{\mu\tau}{S},\; \beta = \frac{\sigma\sqrt{\tau}}{S}$$

and $T/\tau = \inf\{s > 0 : Y_s \geq 1\}$.

$$\mathrm{d}Y_s = (-Y_s + \alpha)\,\mathrm{d}s + \beta\,\mathrm{d}W_s, \qquad Y_0 = 0$$

$$E[Y_s|Y_0 = 0] = \alpha(1 - e^{-s})$$
$$\mathrm{Var}[Y_t|Y_0 = 0] = \frac{1}{2}\beta^2(1 - e^{-2s})$$

Let $f_{T/\tau}(s)$ be the density of T/τ.
An exact expression is only known for $\alpha = 1$:

$$f_{T/\tau}(s)_{\alpha=1} = \frac{2e^{2s}}{\sqrt{\pi}\beta(e^{2s}-1)^{3/2}} \exp\Big(-\frac{1}{\beta^2(e^{2s}-1)}\Big)$$

The maximum likelihood estimator:

$$\alpha = 1: \quad \check{\beta}^2 = \frac{1}{N}\sum_{i=1}^{N}\frac{2}{e^{2s_i}-1}$$

Example: Ornstein-Uhlenbeck process

The Laplace transform of T:

$$E\big[e^{kT/\tau}\big] = \frac{\exp\{\frac{\alpha^2}{2\beta^2}\}D_k\left(\frac{\sqrt{2}\alpha}{\beta}\right)}{\exp\{\frac{(\alpha-1)^2}{2\beta^2}\}D_k\left(\frac{\sqrt{2}(\alpha-1)}{\beta}\right)} = \frac{H_k\left(\frac{\alpha}{\beta}\right)}{H_k\left(\frac{(\alpha-1)}{\beta}\right)}$$

for $k < 0$, where $D_k(\cdot)$ and $H_k(\cdot)$ are parabolic cylinder and Hermite functions, respectively.

Ricciardi & Sato, 1988 derived series expressions for the moments of T. In particular

$$E[T/\tau] = \frac{1}{2}\sum_{n=1}^{\infty}\frac{2^n}{n!}\frac{(1-\alpha)^n - (-\alpha)^n}{\beta^n}\Gamma\Big(\frac{n}{2}\Big)$$

The expression is difficult to work with, especially if $|\alpha| \gg 1$ (strongly sub- or suprathreshold) because of the canceling effects in the alternating series. The expression for the variance includes the digamma function also.

Inoue, Sato & Ricciardi, 1995, proposed computer intensive methods of estimation by using the empirical moments of T.

$$dX_t = \left(-\frac{X_t}{\tau} + \mu\right)dt + \sigma dW_t \;\; ; \;\; X_0 = x_0 = 0;$$

with solution

$$X_t = \mu\tau(1 - e^{-\frac{t}{\tau}}) + \sigma\int_0^t e^{-\frac{(t-s)}{\tau}}dW_s$$

Define the martingale:

$$Y_t = (\mu\tau - X_t)e^{\frac{t}{\tau}} = \mu\tau - \sigma\int_0^t e^{\frac{s}{\tau}}dW_s$$

If $M(t)$ is a martingale, then $E[M(T \wedge t)] = E[M(0)]$

We need more than that:

Doob's Optional-Stopping Theorem

Let T be a stopping time and let $M(t)$ be a uniformly integrable martingale. Then $E[M(T)] = E[M(0)]$.

Y_t is obviously not uniform integrable (UI) (it is equivalent to a Brownian Motion). CLAIM:

$$Y^T(t) := Y(T \wedge t),$$

the process stopped at T, is UI in certain part of the parameter region - particularly we will always assume $(\mu\tau - S) > 0$ (suprathreshold regime).

We show that

$$E[|Y_t^T|^p] < K$$

for all t and some $p > 1$ and some positive $K < \infty$.

First observe that

$$Y_{T\wedge t} = (\mu\tau - X_{T\wedge t})e^{\frac{(T\wedge t)}{\tau}} \geq (\mu\tau - S)e^{\frac{(T\wedge t)}{\tau}} > 0$$

for all t if $\mu\tau > S$ (suprathreshold regime).

Set $p = 2$. We have

$$\begin{aligned} E[|Y_t^T|^2] &= E[(Y_t^T)^2] \\ &= E[(\mu\tau - \sigma \int_0^{T\wedge t} e^{\frac{s}{\tau}} dW_s)^2] \\ &= (\mu\tau)^2 - 0 + \sigma^2 E[(\int_0^{T\wedge t} e^{\frac{s}{\tau}} dW_s)^2] \end{aligned}$$

$$M(t) = (\int_0^t e^{\frac{s}{\tau}} dW_s)^2 - \int_0^t e^{\frac{2s}{\tau}} ds$$

is a martingale due to Itôs isometry:

$$E(\int_0^t f(s,\omega) dW_s)^2 = \int_0^t E[f(s,\omega)^2] ds$$

such that $E[M(T \wedge t)] = E[M(0)] = 0$. This yields

$$\begin{aligned} E[(\int_0^{T\wedge t} e^{\frac{s}{\tau}} dW_s)^2] &= E[\int_0^{T\wedge t} e^{\frac{2s}{\tau}} ds] \\ &= E[\frac{\tau}{2}(e^{\frac{2(T\wedge t)}{\tau}} - 1)] \\ &\leq \frac{\tau}{2} E[e^{\frac{2T}{\tau}}] \end{aligned}$$

Thus, we have:

$$E[|Y_t^T|^2] \quad \leq \quad (\mu\tau)^2 + \sigma^2 \frac{\tau}{2} E[e^{\frac{2T}{\tau}}]$$

We need to show that this is finite.

Define the martingale (to be trusted):

$$Y_2(t) = (\mu\tau - X(t))^2 e^{\frac{2t}{\tau}} + \frac{\tau\sigma^2}{2}(1 - e^{\frac{2t}{\tau}})$$

such that

$$E[Y_2(T \wedge t)] = E[Y_2(0)] = (\mu\tau)^2$$

which yields

$$\begin{aligned} (\mu\tau)^2 &= E[(\mu\tau - X(T \wedge t))^2 e^{\frac{2(T\wedge t)}{\tau}} + \frac{\tau\sigma^2}{2}(1 - e^{\frac{2(T\wedge t)}{\tau}})] \\ &\geq \left((\mu\tau - S)^2 - \frac{\tau\sigma^2}{2} \right) E[e^{\frac{2(T\wedge t)}{\tau}}] + \frac{\tau\sigma^2}{2} \end{aligned}$$

If $(\mu\tau - S)^2 > \frac{\tau\sigma^2}{2}$ then

$$\frac{(\mu\tau)^2 - \frac{\tau\sigma^2}{2}}{(\mu\tau - S)^2 - \frac{\tau\sigma^2}{2}} \quad \geq \quad E[e^{\frac{2(T\wedge t)}{\tau}}].$$

Taking limits on both sides we obtain

$$\frac{(\mu\tau)^2 - \frac{\tau\sigma^2}{2}}{(\mu\tau - S)^2 - \frac{\tau\sigma^2}{2}} \quad \geq \quad \lim_{t\to\infty} E[e^{\frac{2(T\wedge t)}{\tau}}] = E[e^{\frac{2T}{\tau}}]$$

since T is almost surely finite.

BINGO! Doob is good.

If $S < \mu\tau$ (suprathreshold regime) and $(\mu\tau - S)^2 > \frac{\tau\sigma^2}{2}$ then

$$E[Y^T(0)] \quad = \quad E[Y^T(T)]$$

such that

$$\begin{aligned} \mu\tau = E[Y^T(0)] &= E[Y^T(T)] \\ &= E[(\mu\tau - X(T))e^{\frac{T}{\tau}}] \\ &= (\mu\tau - S)E[e^{\frac{T}{\tau}}]. \end{aligned}$$

Beautiful result

$$E[e^{\frac{T_S}{\tau}}] = \frac{\mu\tau}{\mu\tau - S}$$

With a little more work (and more restrictions on parameter space):

$$E[e^{\frac{2T_S}{\tau}}] = \frac{(\mu\tau)^2 - \frac{\tau\sigma^2}{2}}{(\mu\tau - S)^2 - \frac{\tau\sigma^2}{2}}$$

In fact, generally we have (Ditlevsen, 2007):

Let $(\mu, \tau, \sigma) = \theta \in \Theta^{(k)} = \{\theta \,|\, \mu\tau > S, \sqrt{\sigma^2\tau} < (\mu\tau - S)/\lambda^{(k)}\}$ for $k \in \mathbb{N}$, where $\lambda^{(k)}$ is the largest root of the k'th Hermite polynomial. Then

$$E\left[e^{\lambda T/\tau}\right] = \frac{H_\lambda\left(\frac{\mu\tau}{\sigma\sqrt{\tau}}\right)}{H_\lambda\left(\frac{(\mu\tau - S)}{\sigma\sqrt{\tau}}\right)}$$

for $\lambda \le k$, where H_λ is the Hermite function.

k	$\lambda^{(k)}$	$E\left[e^{k\beta T}\right]$
1	0	$\mu\tau/(\mu\tau - S)$
2	$\frac{1}{\sqrt{2}}$	$\left((\mu\tau)^2 - \tau\sigma^2/2\right) / \left((\mu\tau - S)^2 - \tau\sigma^2/2\right)$
3	$\sqrt{\frac{3}{2}}$	$\frac{\mu\tau}{(\mu\tau - S)}\left((\mu\tau)^2 - \frac{3\tau\sigma^2}{2}\right) / \left((\mu\tau - S)^2 - \frac{3\tau\sigma^2}{2}\right)$
4	$\sqrt{\frac{3+\sqrt{6}}{2}}$	$\frac{\left((\mu\tau)^2 - \frac{3\tau\sigma^2}{2}\right)^2 - \frac{3\tau^2\sigma^4}{2}}{\left((\mu\tau - S)^2 - \frac{3\tau\sigma^2}{2}\right)^2 - \frac{3\tau^2\sigma^4}{2}}$

Tabel 1: The first 4 moments of $e^{\beta T}$, where T is the first-passage time of an Ornstein-Uhlenbeck process with parameters $\theta = (\mu, \tau, \sigma)$ through a constant threshold S, which is valid for $\theta \in \Theta^{(k)} = \{\theta \,|\, \mu\tau > S, \sqrt{\tau\sigma^2} < (\mu\tau - S)/\lambda^{(k)}\}$.

Explicit expressions for the parameters

$$\mu = \frac{SE[e^{\frac{T_S}{\tau}}]}{\tau(E[e^{\frac{T_S}{\tau}}] - 1)}$$

$$\sigma^2 = \frac{2S^2\mathrm{Var}[e^{\frac{T_S}{\tau}}]}{\tau(E[e^{\frac{2T_S}{\tau}}] - 1)(E[e^{\frac{T_S}{\tau}}] - 1)^2}$$

Straightforward estimators:

$$\hat{E}[Z] = \frac{1}{n}\sum_{i=1}^{n} e^{t_i/\tau}$$
$$\hat{E}[Z^2] = \frac{1}{n}\sum_{i=1}^{n} e^{2t_i/\tau}$$

where $t_i, i = 1, \ldots, n$, are the i.i.d. observations of the FPT's. Naive estimators of the parameters could then be

$$\hat{\mu} = \frac{S(\frac{1}{n}\sum_{i=1}^{n} e^{t_i/\tau})}{\tau(\frac{1}{n}\sum_{i=1}^{n} e^{t_i/\tau} - 1)}$$
$$\hat{\sigma}^2 = \frac{2S^2((\frac{1}{n}\sum_{i=1}^{n} e^{2t_i/\tau}) - (\frac{1}{n}\sum_{i=1}^{n} e^{t_i/\tau})^2)}{\tau((\frac{1}{n}\sum_{i=1}^{n} e^{2t_i/\tau}) - 1)((\frac{1}{n}\sum_{i=1}^{n} e^{t_i/\tau}) - 1)^2}.$$

In Ditlevsen & Lansky, 2005, the following moments were derived

$$E[e^{T/\tau}] = \frac{\alpha}{\alpha - 1} \quad \text{if } \alpha > 1$$
$$E[e^{2T/\tau}] = \frac{\alpha^2 - \beta^2/2}{(\alpha-1)^2 - \beta^2/2} \quad \text{if } \alpha - 1 > \frac{\beta}{\sqrt{2}}$$

which provides *explicit* estimators

$$\hat{\alpha} = \frac{Z_1}{Z_1 - 1}, \quad \hat{\beta}^2 = \frac{2(Z_2 - Z_1^2)}{(Z_2 - 1)(Z_1 - 1)^2}$$

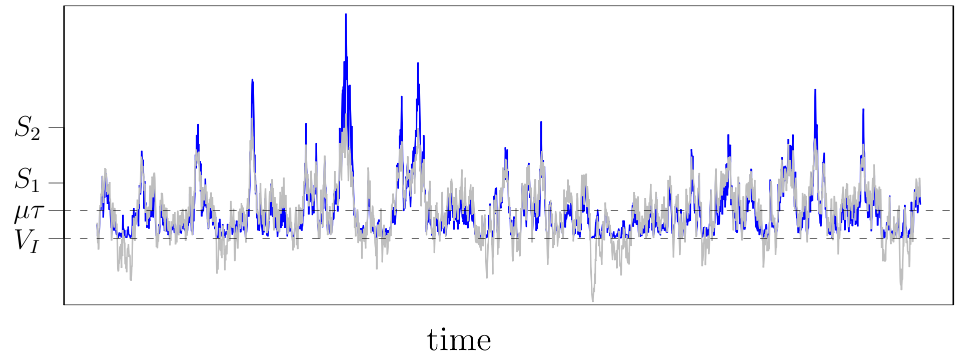
where

$$Z_1 = \frac{1}{N}\sum_{i=1}^{N} e^{s_i}, \quad Z_2 = \frac{1}{N}\sum_{i=1}^{N} e^{2s_i}$$

Feller process

$$\mathrm{d}Y_s = (-Y_s + \alpha)\,\mathrm{d}s + \frac{\beta}{\sqrt{\alpha}}\sqrt{Y_s}\,\mathrm{d}W_s$$

$$E[Y_s|Y_0 = y_0] = \alpha + (y_0 - \alpha)e^{-s}$$
$$\mathrm{Var}[Y_s|Y_0 = y_0] = \frac{\beta^2}{2}(1 - e^{-s})\Big[1 + \Big(\frac{2y_0}{\alpha} - 1\Big)e^{-s}\Big]$$



Ditlevsen & Lansky, 2006 give the moments

$$E[e^{T/\tau}] = \frac{\alpha - y_0}{\alpha - 1} \quad \text{if} \quad \alpha > 1$$

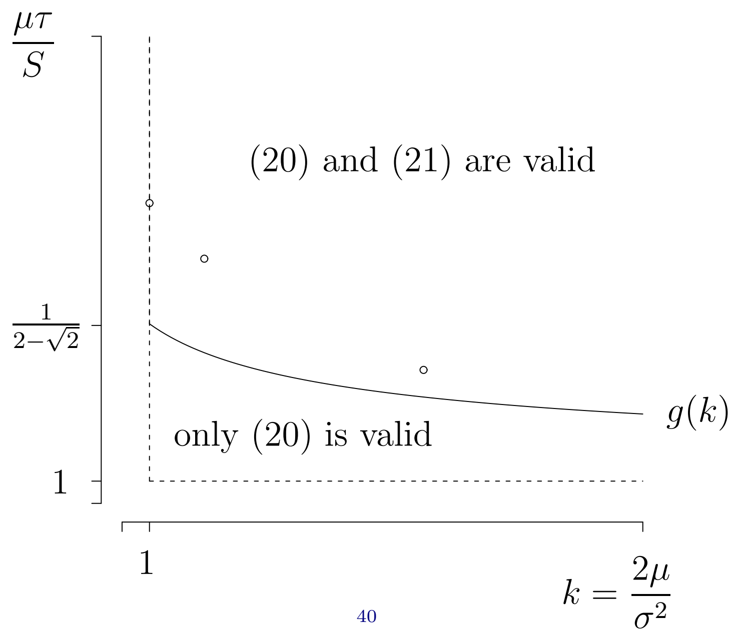
$$E[e^{2T/\tau}] = \frac{2\alpha(\alpha - y_0)^2 + \beta^2(\alpha - 2y_0)}{2\alpha(\alpha-1)^2 + \beta^2(\alpha - 2)} \quad \text{if} \sqrt{1 + 2(\alpha/\beta)^2} \quad < 1 + \frac{2\alpha(\alpha-1)}{\beta^2}$$

Moment estimators:

$$\hat{\alpha} = \frac{Z_1 - y_0}{Z_1 - 1}$$

and

$$\hat{\beta}^2 = \frac{2(1-y_0)^2(Z_2 - Z_1^2)}{2(Z_1-1)(Z_2-y_0) - (Z_1-y_0)(Z_2-1)}\,\hat{\alpha}$$



The Fortet integral equation

Set $S = 1$. The probability

$$P[X_t > 1 \,|\, X_0 = x_0] \;=\; \int_{y>1} f_\theta(t, x_0, y)dy \;=\; 1 - F_\theta(t, x_0, 1) \;=\; \text{LHS}(t)$$

can alternatively be calculated by the transition integral

$$P[X_t > 1 \,|\, X_0 = x_0] \;=\; \int_0^t p_\theta(u)\big(1 - F_\theta(t-u, 1, 1)\big)du \;=\; \text{RHS}(t)$$

Parameter estimation

Sample $t_1, \ldots, t_n$ of independent observations of T. Fix θ.

RHS can be estimated at t from the sample by the average

$$\text{RHS}(t;\theta) = \int_0^t p_\theta(u)\big(1 - F_\theta(t-u, 1, 1)\big)du$$

$$\approx$$

$$\text{RHS}_{\text{emp}}(t;\theta) = \frac{1}{n}\sum_{i=1}^n \big(1 - F_\theta(t - t_i, 1, 1)\big)1_{\{t_i \le t\}}$$

since for fixed t it is the expected value of

$$1_{T\in[0,t]}\big(1 - F_\theta(t - T, 1, 1; \theta)\big)$$

with respect to the distribution of T.

Parameter estimation

Error measure:

$$L(\theta) = \sup_{t>0} |(\mathrm{RHS}_{\mathrm{emp}}(t) - \mathrm{LHS}(t))/\omega|$$

where $\omega = \sup_{t>0}(1 - F_\theta(t, x_0, 1; \theta))$.

Estimator:

$$\tilde{\theta} = \arg\min_{\theta} L(\theta)$$

(Ditlevsen and Ditlevsen 2008; Ditlevsen and Lansky 2007)

(Review paper: Lansky and Ditlevsen 2008)

Example: Ornstein-Uhlenbeck process

Let $f(s)$ be the density function for the time t/τ from zero to the first crossing of the level 1 by Y. The probability

$$P[Y(s) > 1] = \Phi\Big(\frac{\alpha(1 - e^{-s}) - 1}{\sqrt{1 - e^{-2s}}\, \beta/\sqrt{2}} \Big)$$

can alternatively be calculated by the transition integral

$$P[Y(s) > 1] = \int_0^s f(u)\, \Phi\left(\frac{\alpha - 1}{\beta/\sqrt{2}} \frac{1 - e^{-(s-u)}}{\sqrt{1 - e^{-2(s-u)}}} \right) \mathrm{d}u$$

Parameter estimation

$$\begin{aligned} &\mathrm{LHS}(s) = \\ &\Phi\Big(\frac{\alpha(1 - e^{-s}) - 1}{\sqrt{1 - e^{-2s}}\, \beta/\sqrt{2}} \Big) = \int_0^s f(u)\, \Phi\left(\frac{\alpha - 1}{\beta/\sqrt{2}} \sqrt{\frac{1 - e^{-(s-u)}}{1 + e^{-(s-u)}}} \right) \mathrm{d}u \\ &= \mathrm{RHS}(s) \end{aligned}$$

Sample: $s_1 \leq s_2 \leq \ldots \leq s_n$, iid observations of T/τ.

Parameter estimation

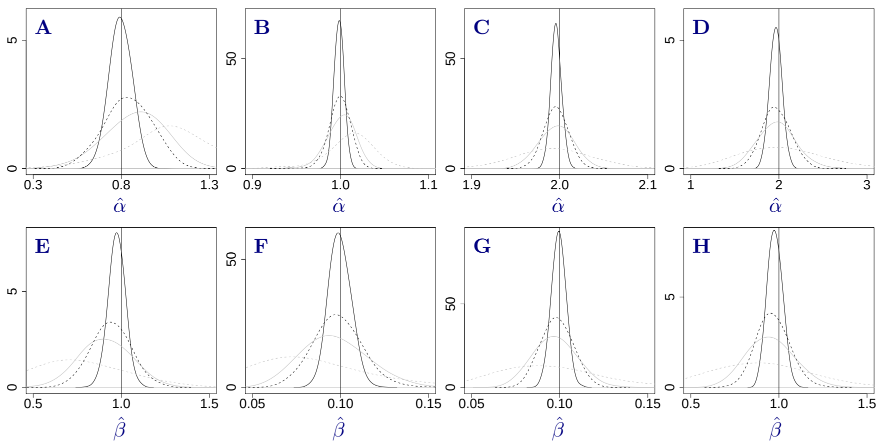
Sample: $s_1 \leq s_2 \leq \ldots \leq s_n$, iid observations of T/τ.

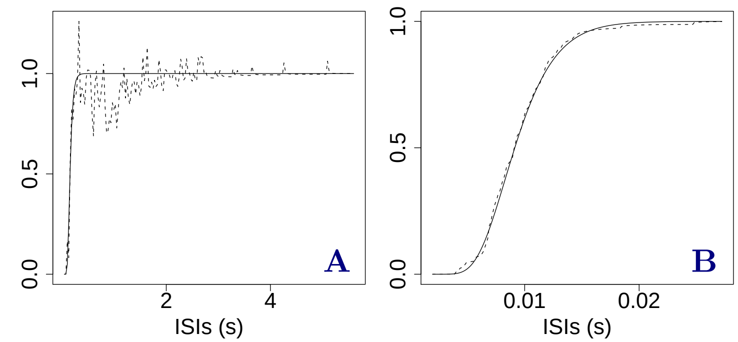
$$\mathrm{RHS}(s) \approx \frac{1}{n} \sum_{i=1}^{n} \Phi\left(\frac{\alpha - 1}{\beta/\sqrt{2}} \sqrt{\frac{1 - e^{-(s-s_i)}}{1 + e^{-(s-s_i)}}} \right) 1_{\{s_i \leq s\}}$$

since it is the expected value of

$$1_{U \in [0,s]} \Phi\left(\frac{\alpha - 1}{\beta/\sqrt{2}} \sqrt{\frac{1 - e^{-(s-U)}}{1 + e^{-(s-U)}}} \right)$$

with respect to the distribution of $U = T/\tau$ for given α and β.





Figur 1: Auditory neurons. A: Spontaneous record; $\hat{\alpha} = 0.85; \hat{\beta} = 0.09$. B: Stimulated record; $\hat{\alpha} = 4.8; \hat{\beta} = 0.63$. Note different time axes.

Feller process

$$\mathrm{d}Y_s = (-Y_s + \alpha)\ \mathrm{d}s + \frac{\beta}{\sqrt{\alpha}}\sqrt{Y_s}\,\mathrm{d}W_s$$

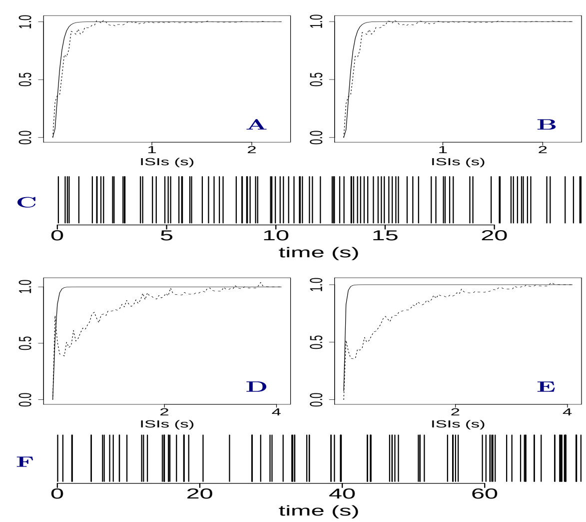
$$E[Y_s|Y_0 = y_0] = \alpha + (y_0 - \alpha)e^{-s}$$

$$\mathrm{Var}[Y_s|Y_0 = y_0] = \frac{\beta^2}{2}(1 - e^{-s})\Big[1 + \Big(\frac{2y_0}{\alpha} - 1\Big)e^{-s}\Big]$$

Chapman-Kolmogorov integral equation:

$$1 - F_{\chi^2}[a(s), \nu, \delta(s, y_0)] = \int_0^s f(u)\{1 - F_{\chi^2}[a(s-u), \nu, \delta(s-u, 1)]\}\,\mathrm{d}u$$

$a(s) = (4\alpha)/\beta^2(1 - e^{-s})$, $\delta(s, y_0) = (4\alpha y_0/\beta^2)[e^{-s}/(1 - e^{-s})]$ and $\nu = 4(\alpha/\beta)^2$.



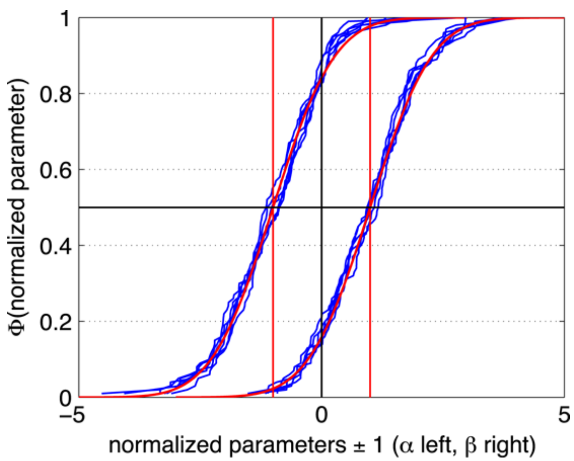


Fig. 2. Normalized empirical distribution functions of the sample of 100 joint estimates of α and β compared to the standardized normal distribution function.

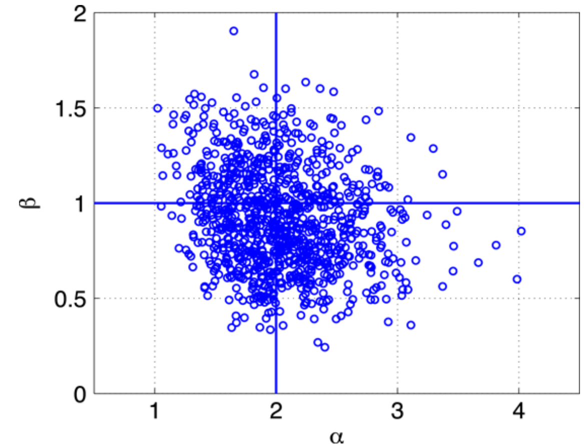


Fig. 3. Scatterplots of the 996 pairs of estimates of (α, β), each estimated from a sample of 10 simulated first-passage times corresponding to the true values $\alpha = 2$ and $\beta = 1$.

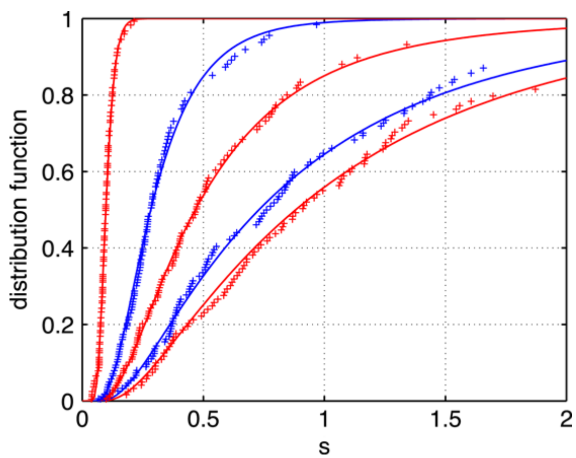
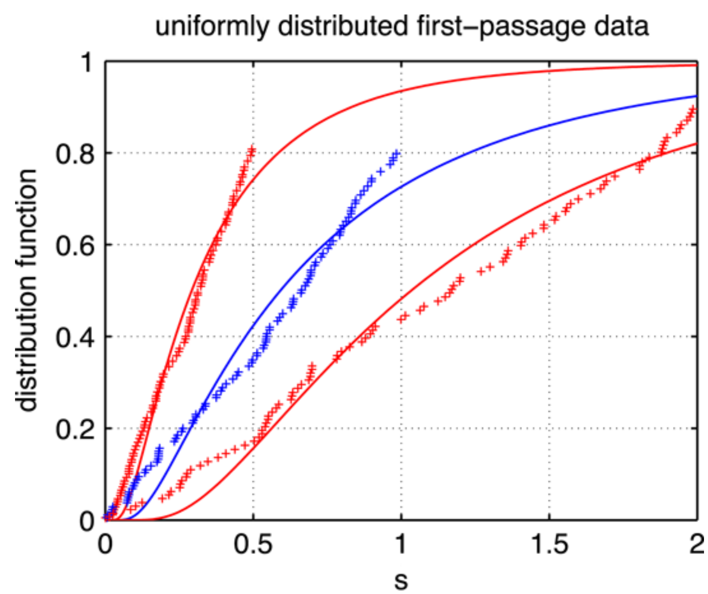
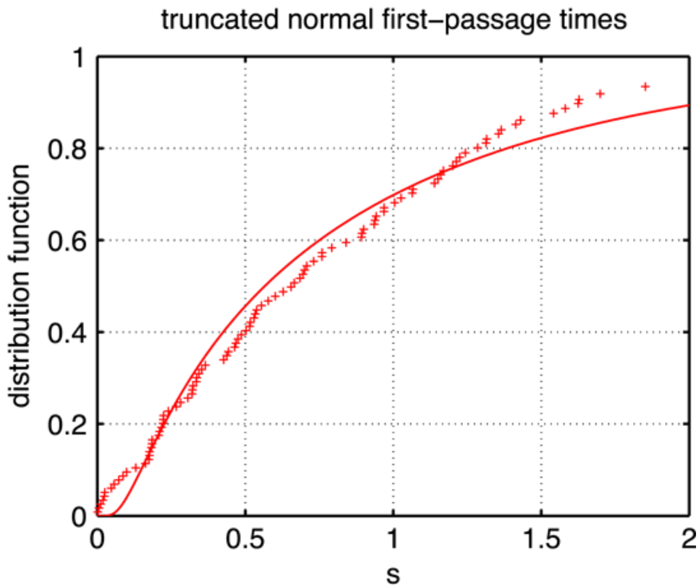
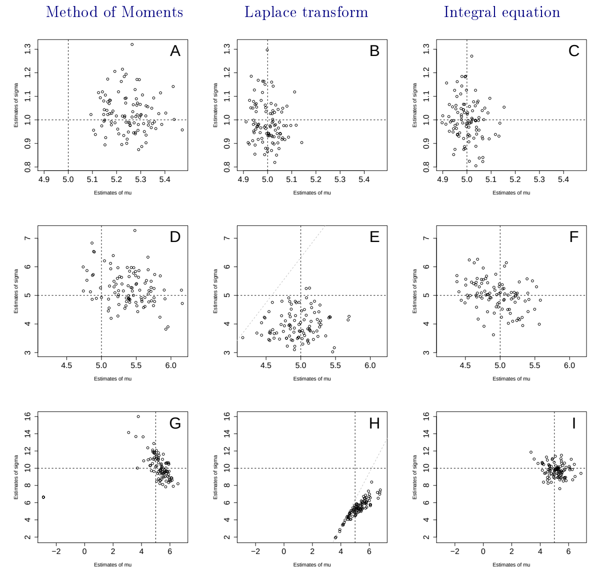


Fig. 5. Comparison of the (normalized) left-hand side of the integral equation (25) (smooth curves) with the empirical (normalized) right-hand side given by (26) for five simulated samples of 100 first-passage times of the OU process of the level 1 corresponding to the true α-values 1, 2, 3, 4, 11, respectively, and the true $\beta = 1$ (right to left). For these samples the estimates of (α, β) according to







regime	$\beta = 1$	statistics of 100 estimates: average $\pm$ SSD	
	$\alpha =$	$\hat{\alpha}$	$\tilde{\alpha}$
subthreshold	0.8		0.79 ± 0.09
threshold	1	1.10 ± 0.06	1.00 ± 0.08
suprathreshold	2	1.99 ± 0.10	1.98 ± 0.11
suprathreshold	3	2.97 ± 0.09	2.95 ± 0.10
suprathreshold	4	3.94 ± 0.12	3.90 ± 0.11
$\approx$ Wiener	11	10.96 ± 0.11	9.88 ± 0.15

regime	$\beta = 1$	statistics of 100 estimates: average $\pm$ SSD	
	$\alpha =$	$\hat{\beta}$	$\tilde{\beta}$
subthreshold	0.8		0.94 ± 0.10
threshold	1		0.93 ± 0.10
suprathreshold	2	0.64 ± 0.10	0.95 ± 0.08
suprathreshold	3	0.48 ± 0.05	0.96 ± 0.10
suprathreshold	4	0.39 ± 0.04	0.92 ± 0.09
$\approx$ Wiener	11	0.22 ± 0.02	1.46 ± 0.16