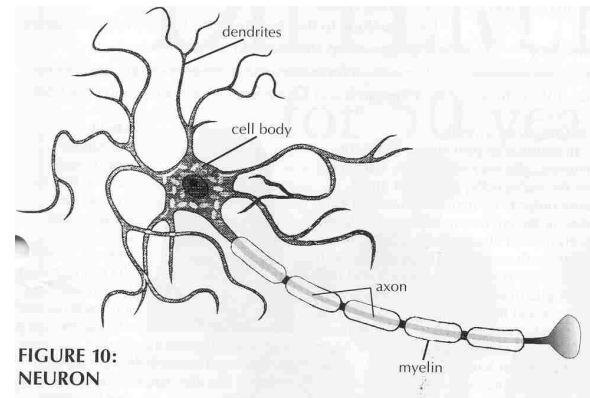


Parameter estimation in diffusion processes from observations of first hitting-times

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

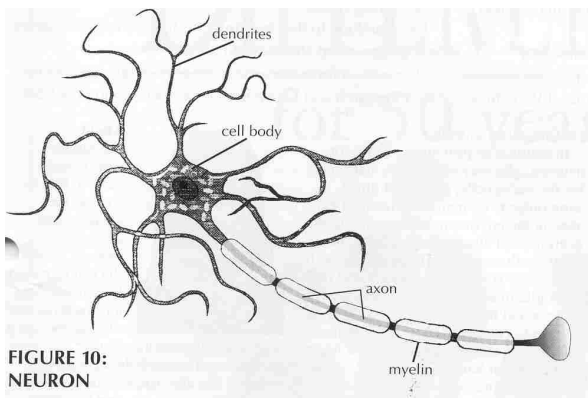
Summer school 4–12 August 2008, Middelfart, Denmark

Motivating example: Neurons (nerve cells)

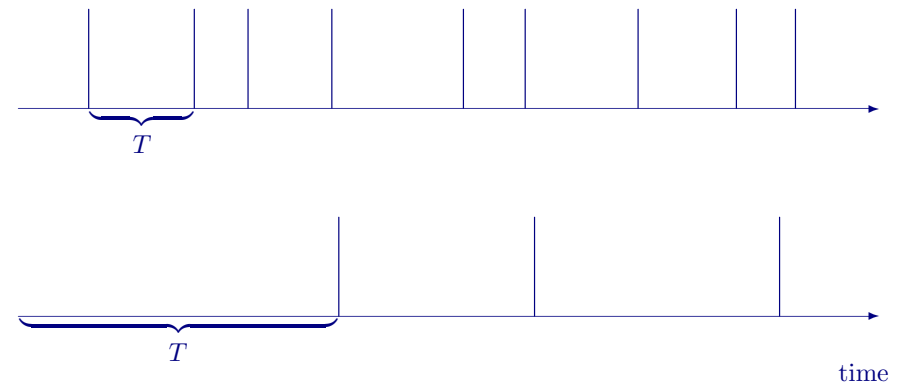


1

Motivating example: Neurons (nerve cells)



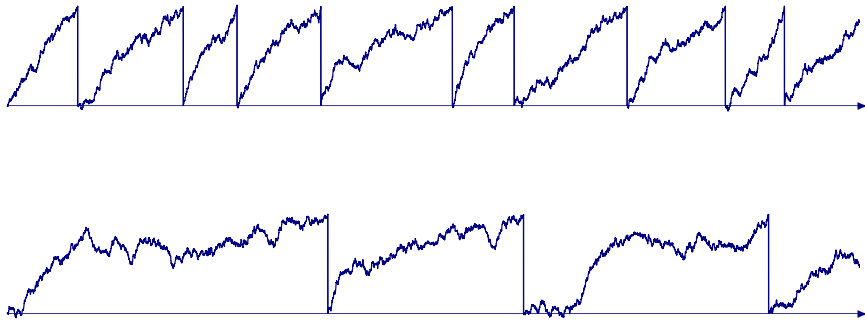
Data: spiketrains



1

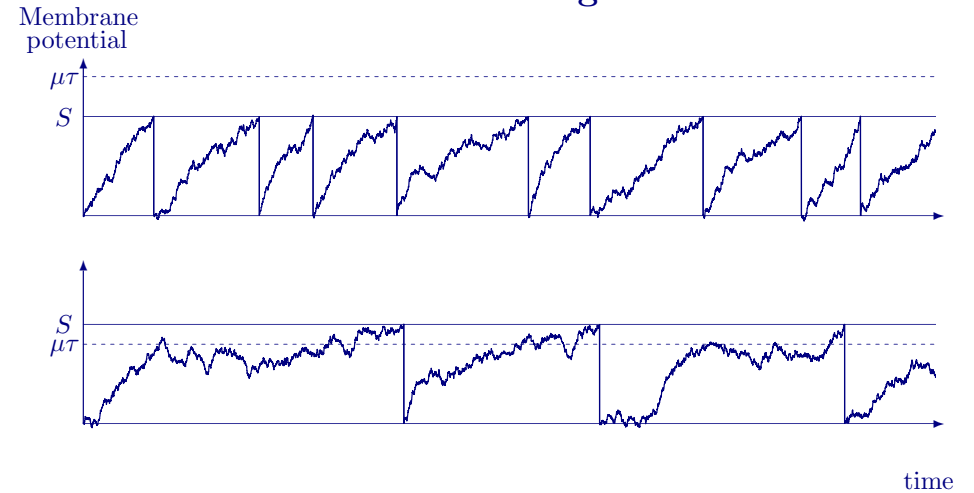
2

Underlying process



3

Threshold regimes



4

The model

$$dX_t = \mu(X_t) dt + \sigma(X_t) dW(t) ; X_0 = x_0$$

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*

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

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

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

5

Data

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

Data: $\{t_1, t_2, \dots, t_n\}$ 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.

6

Estimation

$$dX_t = \mu(X_t, \theta) dt + \sigma(X_t, \theta) dW(t) \quad ; \quad \theta \in \Theta \subseteq \mathbb{R}^p$$

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

How do we estimate θ ?

7

Example: Brownian motion with drift

$$dX_t = \mu dt + \sigma dW(t) \quad ; \quad \mu > 0, \sigma > 0 \quad ; \quad X_0 = 0 < S$$

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

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

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

9

Maximum likelihood estimation

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

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

Recall:

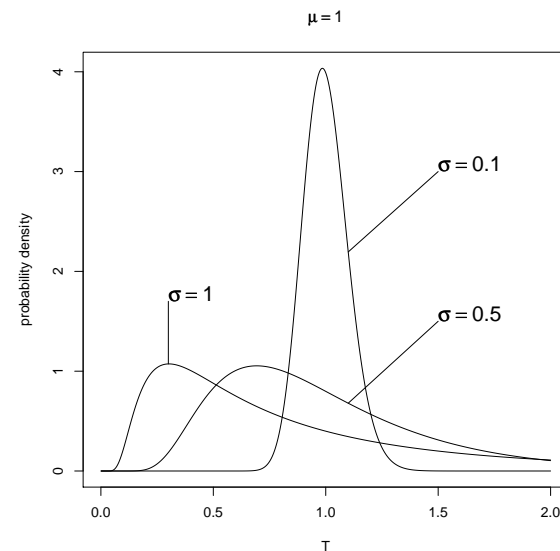
$$\text{Likelihood function:} \quad L_n(\theta) = \prod_{i=1}^n p_\theta(t_i)$$

$$\text{Log-likelihood function:} \quad \log L_n(\theta) = \sum_{i=1}^n \log p_\theta(t_i)$$

$$\text{Score function(s):} \quad \partial_\theta \log L_n(\theta) = \sum_{i=1}^n \partial_\theta \log p_\theta(t_i)$$

$$\text{Estimator } \hat{\theta} \text{ is such that} \quad \partial_\theta \log L_n(\hat{\theta}) = 0$$

8



10

Score functions:

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

Maximum likelihood estimators:

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

where

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

11

The conditional expectation is

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

The conditional variance is

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

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

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

13

Example: The Ornstein-Uhlenbeck model

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

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

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

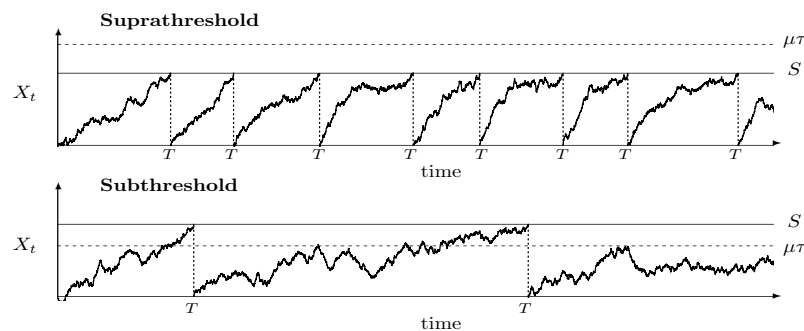
x_0 : initial voltage (the reset value following a spike)

12

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))



14

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

Assumed known:

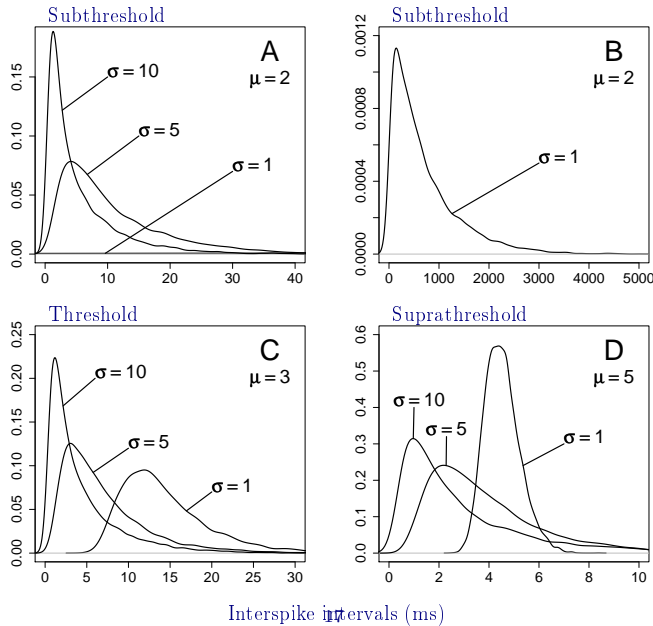
Intrinsic or characteristic parameters of the neuron: τ, x_0, S

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

To be estimated:

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

15



Example: Ornstein-Uhlenbeck process

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

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):

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

16

We reformulate to the equivalent dimensionless form

$$d\left(\frac{X_t}{S}\right) = \left(-\frac{X_t}{S} + \frac{\mu\tau}{S}\right) d\left(\frac{t}{\tau}\right) + \frac{\sigma\sqrt{\tau}}{S} d\left(\frac{W_t}{\sqrt{\tau}}\right)$$

or

$$dY_s = (-Y_s + \alpha) ds + \beta dW_s, \quad Y_0 = 0$$

where

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

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

18

$$dY_s = (-Y_s + \alpha) ds + \beta dW_s, \quad Y_0 = 0$$

$$E[Y_s | Y_0 = 0] = \alpha(1 - e^{-s})$$

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

Let $f_{T/\tau}(s)$ be the density of T/τ .

An exact expression is only known for $\alpha = 1$:

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

The maximum likelihood estimator:

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

19

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

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

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 .

21

Example: Ornstein-Uhlenbeck process

The Laplace transform of T :

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

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

20

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

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:

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

22

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 $E[M(T)] = E[M(0)]$.

23

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

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

25

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 $K < \infty$.

24

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

is a martingale due to Itô's 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

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

26

Thus, we have:

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

We need to show that this is finite.

27

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

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

Taking limits on both sides we obtain

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

since T is almost surely finite.

29

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

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

28

BINGO! Doob is good.

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

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

such that

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

30

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):

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

31

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

Table 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 $\theta \in \Theta^{(k)} = \{\theta \mid \mu\tau > S, \sqrt{\tau\sigma^2} < (\mu\tau - S)/\lambda^{(k)}\}$.

33

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

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

Then

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

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

32

Explicit expressions for the parameters

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

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

34

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

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

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

35

Feller process

$$dY_s = (-Y_s + \alpha) ds + \frac{\beta}{\sqrt{\alpha}} \sqrt{Y_s} dW_s$$

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

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

37

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

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

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

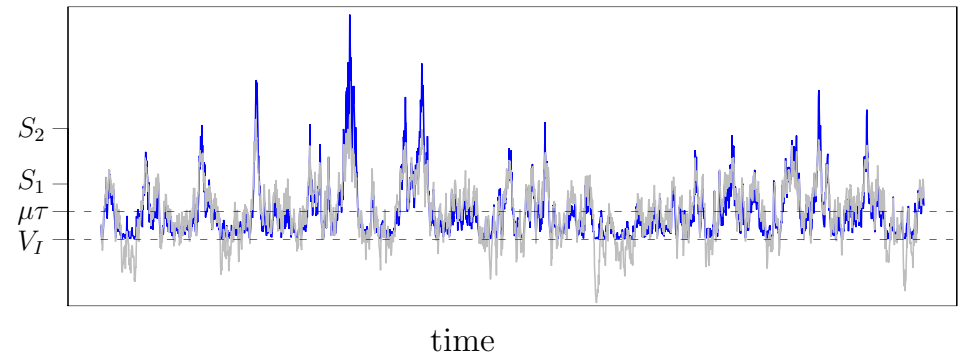
which provides *explicit* estimators

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

where

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

36



38

Ditlevsen & Lansky, 2006 give the moments

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

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

Moment estimators:

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

and

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

39

The Fortet integral equation

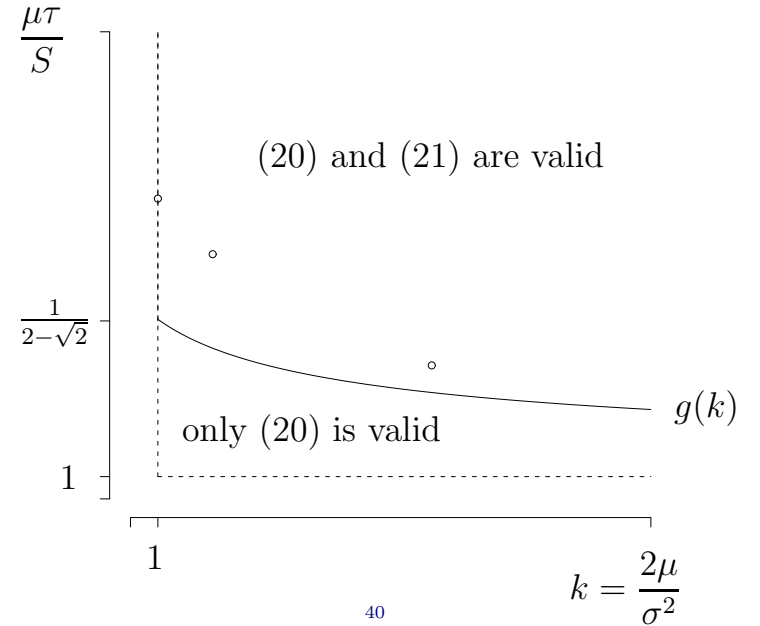
Set $S = 1$. The probability

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

can alternatively be calculated by the transition integral

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

41



40

Parameter estimation

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

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

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

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

since for fixed t it is the expected value of

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

with respect to the distribution of T .

42

Parameter estimation

Error measure:

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

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)

43

Parameter estimation

LHS(s) =

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

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

45

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

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

can alternatively be calculated by the transition integral

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

44

Parameter estimation

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

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

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 .

46

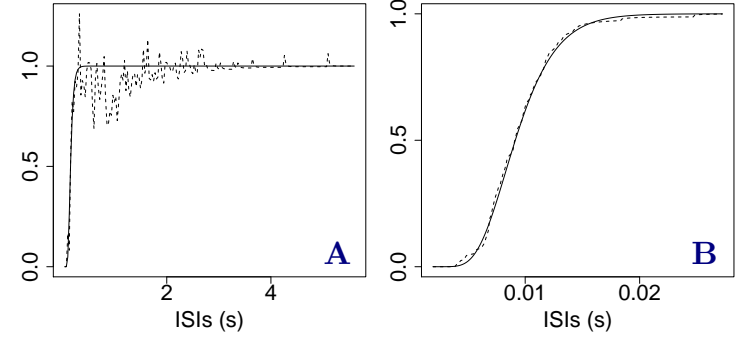
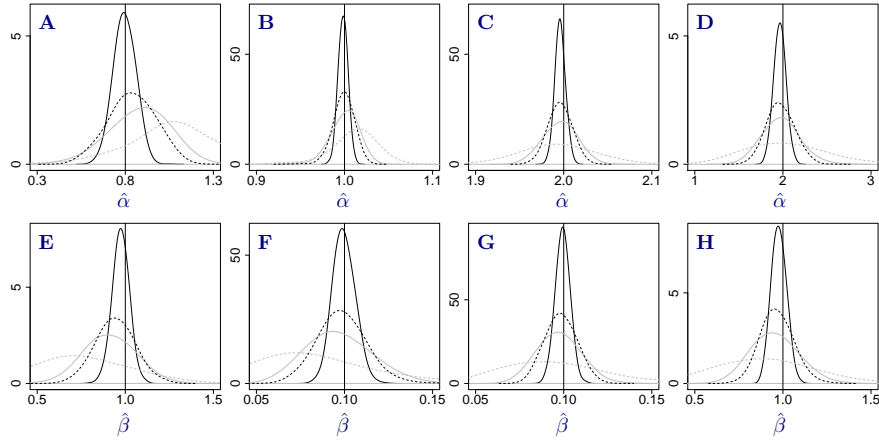


Figure 1: Auditory neurons. A: Spontaneous record; $\hat{\alpha} = 0.85$; $\hat{\beta} = 0.09$. B: Stimulated record; $\hat{\alpha} = 4.8$; $\hat{\beta} = 0.63$. Note different time axes.

47

Feller process

$$dY_s = (-Y_s + \alpha) ds + \frac{\beta}{\sqrt{\alpha}} \sqrt{Y_s} dW_s$$

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

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

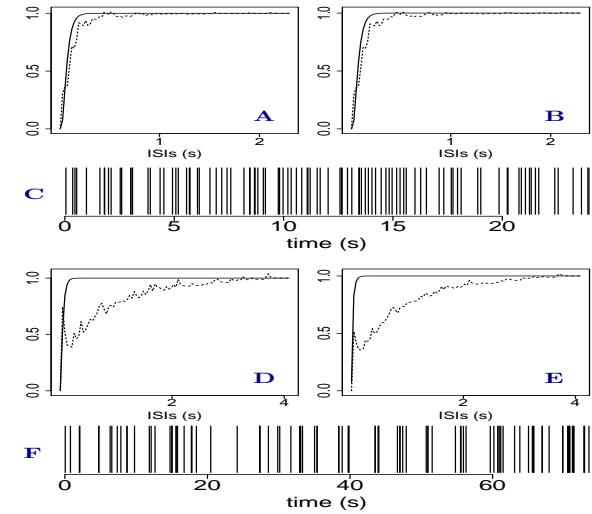
Chapman-Kolmogorov integral equation:

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

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

49

48



50

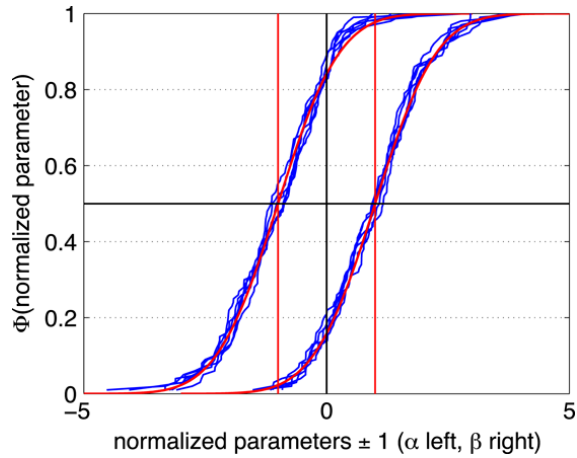


Fig. 2. Normalized empirical distribution functions of the sample of 100 joint estimates of α and β compared to the standardized normal distribution function.

51

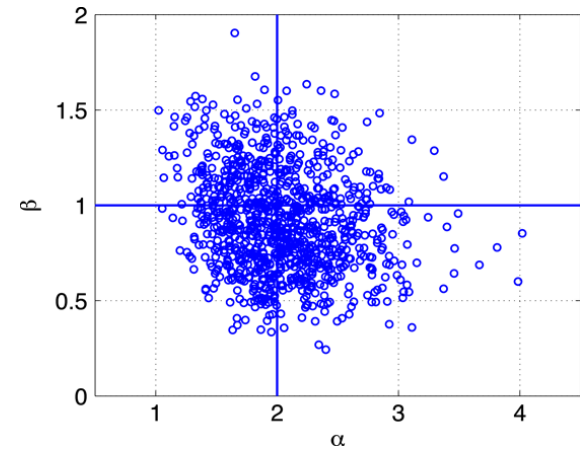


Fig. 3. Scatterplots of the 996 pairs of estimates of (α, β) , each estimated from a sample of 10 simulated first-passage times corresponding to the true values $\alpha = 2$ and $\beta = 1$.

52

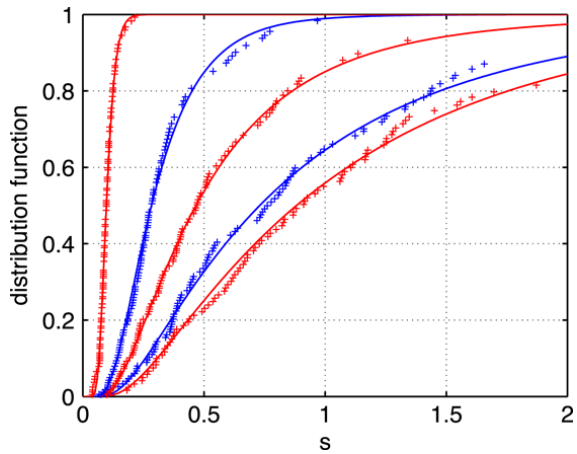
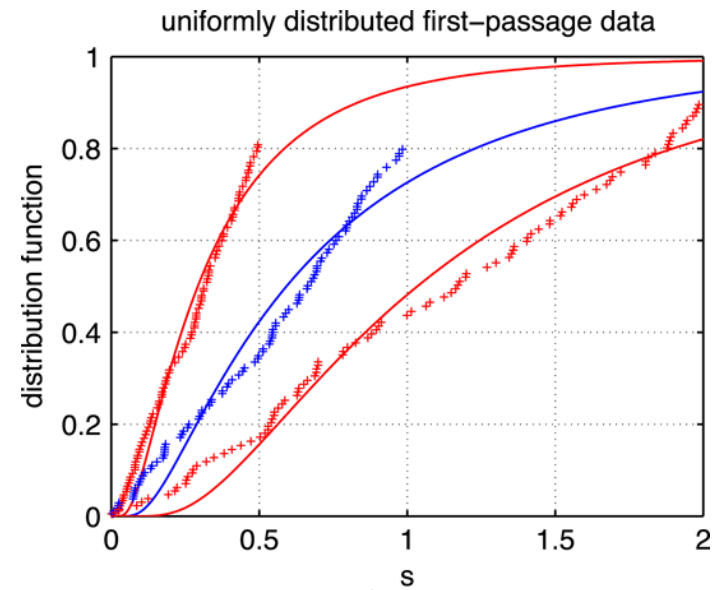
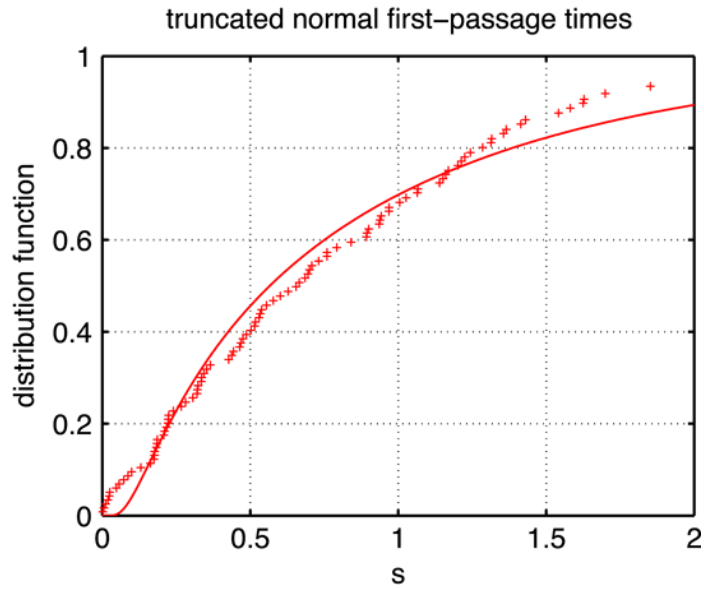


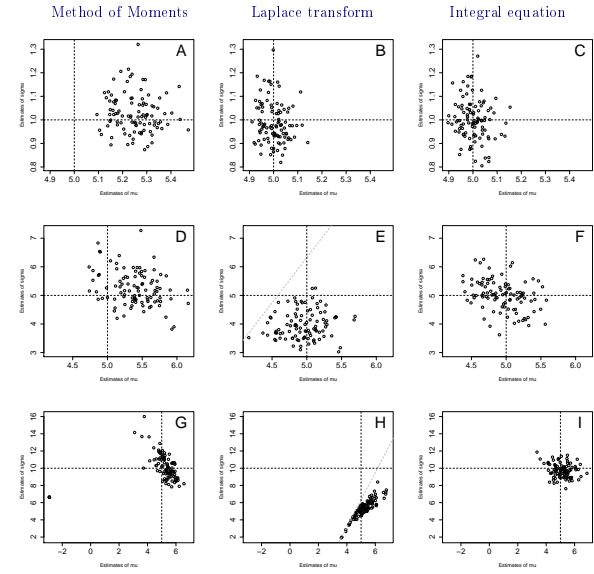
Fig. 5. Comparison of the (normalized) left-hand side of the integral equation (25) (smooth curves) with the empirical (normalized) right-hand side given by (26) for five simulated samples of 100 first-passage times of the OU process of the level 1 corresponding to the true α -values 1, 2, 3, 4, 11, respectively, and the true $\beta = 1$ (right to left). For these samples the estimates of (α, β) according to (20) are: (1.012, 0.999), (1.977, 0.999), (2.977, 0.999), (3.977, 0.999), (10.999, 0.999).



54



55



56

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

57

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

58