# To which extent is the membrane potential in a neuron between successive spikes adequately modelled by a (continuous) semimartingale?

Reinhard Höpfner

Johannes Gutenberg Universität Mainz
www.mathematik.uni-mainz.de/∼hoepfner

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# semimartingale models for the membrane potential in a neuron between successive spikes

huge litterature modelling the membrane potential between successive spikes as a time homogeneous diffusion, e.g. mean-reverting OU

(overviews in Tuckwell 89 and Lansky-Sato 99, see also Lansky-Sacerdote 01, Ditlevsen-Lansky 05, ...)

or mean reverting CIR

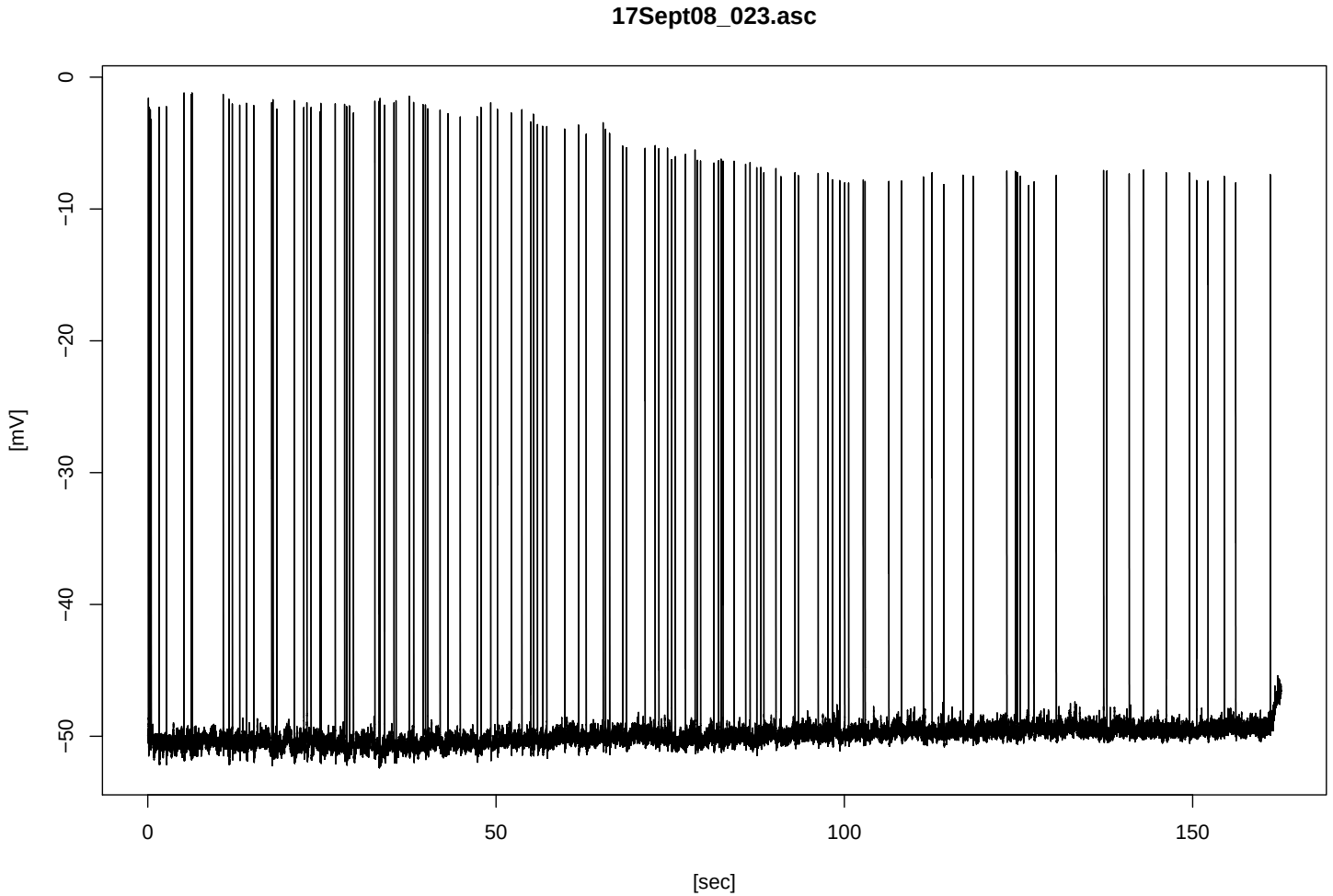
(Lansky-Lanska 87, Giorno-Lansky-Nobile-Ricciardi 88, Lansky-Sacerdote-Tomassetti 95, Ditlevsen-Lansky 06, Brodda-Höpfner 06, ...)

in many data sets, evidence that input terms in the drift are strongly varying with time, and some indication that there might be jumps ...

look to Ito semimartingale models for the membrane potential between successive spikes, and ask questions :

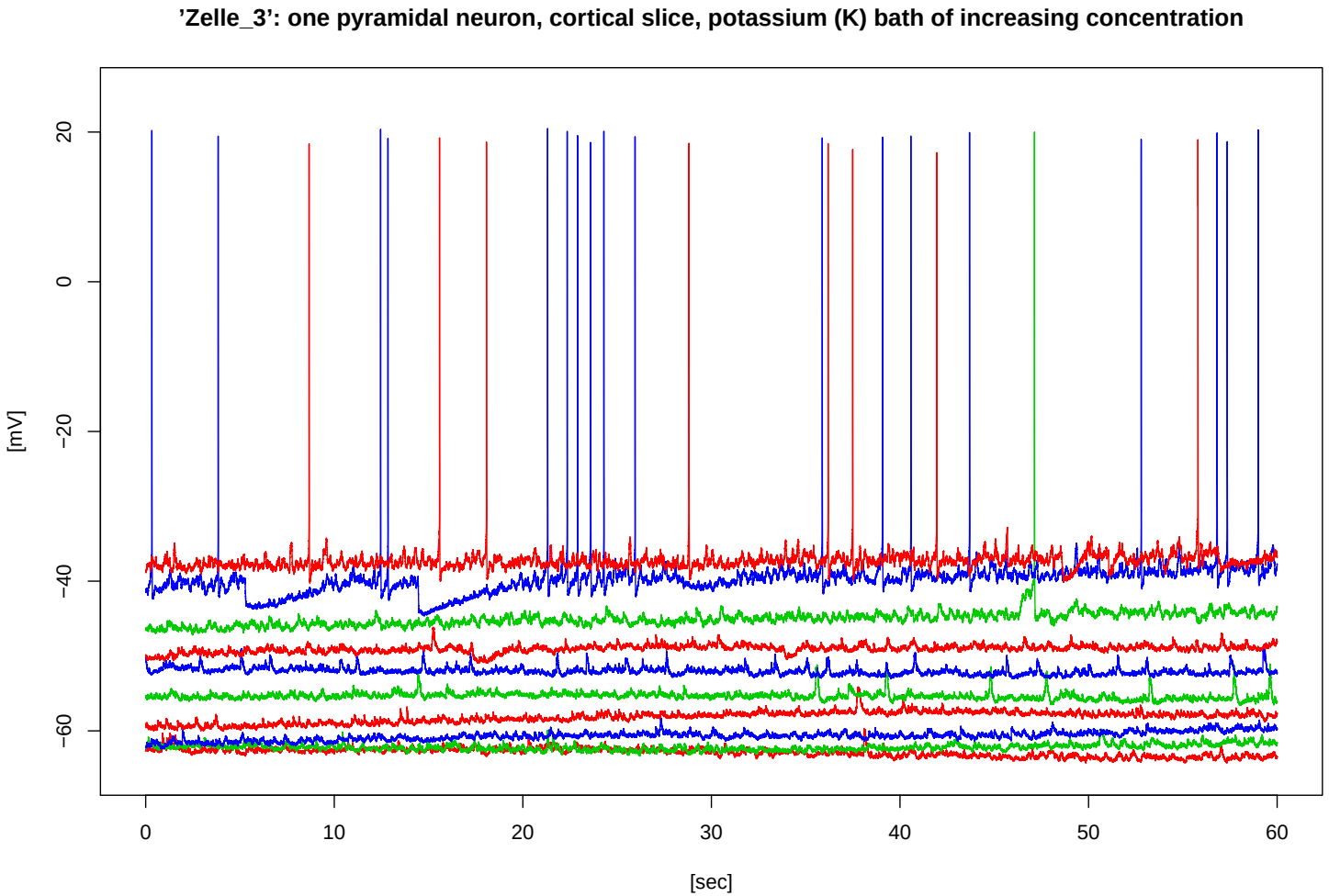
- CIR, OU, ... models, continuous or with jumps, time-homogeneous or not
- model validation relative to shape of diffusion coefficient and drift
- model validation relative to the semimartingale hypothesis

example 1 : the membrane potential in a pyramidal neuron emitting spikes




data : Kilb and Luhmann, Institute of Physiology, University of Mainz

example 2 : one pyramidal neuron under different experimental conditions, network activity stimulated by potassium (K) bath, increasing concentration




data : Luhmann and Kilb, Institute of Physiology, University of Mainz

CIR type model $(V_t)_{t\geq 0}$ for the membrane potential between successive spikes :

$$dV_t \;=\; (f(t) - V_t)\,\tau dt \;+\; \int y\,\mu(dt, dy) \;+\; \sigma\sqrt{(V_t - K_0)^+}\,\sqrt{\tau}\,dW_t$$

with constants $\sigma, \tau > 0$, reference levels $K_0 < K_R < K_E$

- $K_E$ : excitation threshold
- $K_R$ : resting level ( := mean value for m.p. in absence of external stimulus)
- $K_0$ : lower bound for possible values of the membrane potential

deterministic functions of time

$$f : [0,\infty) \to [K_R, K_E] \;, \quad \widetilde{f} : [0,\infty) \to [0, C]$$

modelling external stimulus or degree of activity in the network, and

$$\text{PRM}\;\; \mu(dt, dy) \;\; \text{on} \;\; [0,\infty)\times(0, c] \;\; \text{with intensity} \;\; \widetilde{f}(t)\,\tau dt\,\nu(dy)$$

with measure $\nu(dy)$ $\sigma$-finite on $(0, c]$ such that $\int_{(0,c]} y\,\nu(dy) < \infty$

(Poisson random measure $\mu$ independent of Brownian motion $W$ ;
rate of decay $\tau$ $\longleftrightarrow$ 'membrane time constant' $\frac{1}{\tau}$ for biologists)

time inhomogeneous jump diffusion $(V_t)_t$ as defined above :

proposition 1 : pathwise uniqueness holds, and the m.p. shifted by $K_0$

$$(V_t - K_0)_{t \geq 0}$$

allows for explicit Laplace transforms

$$\lambda \longrightarrow E\left(e^{-\lambda(V_t - K_0)} \mid (V_s - K_0) = x\right) = \int e^{-\lambda y} P_{s,t}(x, dy)$$

for the transition probabilities, given for fixed $x$, $s < t$ by

$$\lambda \longrightarrow \exp\left(-x\Psi_{s,t}(\lambda) - \int_s^t \left\{[f(v) - K_0]\,\Psi_{v,t}(\lambda) + \widetilde{f}(v)\,\widetilde{\Psi}_{v,t}(\lambda)\right\}\tau dv\right)$$

$$\Psi_{v,t}(\lambda) = \frac{e^{-\tau(t-v)}\,\lambda}{1 + \lambda\frac{\sigma^2}{2}(1 - e^{-\tau(t-v)})} \quad , \quad \widetilde{\Psi}_{v,t}(\lambda) = \int [1 - e^{-y\Psi_{v,t}(\lambda)}]\,\nu(dy)$$

in analogy to results of Kawazu-Watanabe TPA 71 for time-homogeneous case

(Kawazu-Watanabe 71, Dawson-Li 06, Fu-Li 08, Höpfner 09)

remark 1 : i) special case $f(\cdot) \equiv f$, $\widetilde{f}(\cdot) \equiv \widetilde{f}$ constant : then jump diffusion $(V_t - K_0)_{t \geq 0}$ has invariant law with LT

$$\lambda \longrightarrow \exp\left( - \int_{-\infty}^{t} \left\{ [f - K_0]\, \Psi_{v,t}(\lambda) + \widetilde{f}\, \widetilde{\Psi}_{v,t}(\lambda) \right\} \tau dv \right)$$

independent of $t$ and $\tau$ : first term is LT of the Gamma law $\Gamma\left(\frac{2}{\sigma^2}[f - K_0]\,,\, \frac{2}{\sigma^2}\right)$, second term corresponds to a space-time Poisson mixture of decay processes

('classical' mean reverting CIR models : $f(\cdot) \equiv f$, no jumps $\widetilde{f}(\cdot) \equiv 0$)

ii) special case where $f(\cdot)$, $\widetilde{f}(\cdot)$ are $T$-periodic functions :
have a $T$-periodic semigroup, an invariant probability on the canonical space $C[0, T]$ for $T$-segments in the path of the process, and Harris-recurrence of the Markov chain of $T$-segments : thus we can obtain limit theorems for a large class of functionals of the process $(V_t - K_0)_{t \geq 0}$ (Höpfner-Kutoyants 10)

time homogeneous CIR gives quite good fit for the membrane potential data of example 1 (17Sept08_023) and for the spiking levels 8+9+10 in example 2 (Zelle_3_K_10, K_12 , K_15)

among the non-spiking levels 1–7 in example 2, some show good fit to OU type and P type ('bowl shaped diffusion coefficient') diffusions, often with marked time dependence for the input term in the drift

## short remarks on nonparametric statistical inference

restriction to time homogenous model without jumps : assume that a diffusion

$$dX_t \;:=\; b(X_t)\,dt \;+\; \sigma(X_t)\,dW_t\;, \quad t \in [T_0, T_1]$$

is observed on a discrete time grid with suitably small step size $\widetilde{\Delta}$

$$X_{i\widetilde{\Delta}}\;,\; i_0 \le i \le i_1\;, \quad i_0 := \lceil \frac{T_0}{\widetilde{\Delta}} \rceil\;,\; i_1 := \lfloor \frac{T_1}{\widetilde{\Delta}} \rfloor$$

in real data sets : $\widetilde{\Delta} = M\Delta$, $\Delta$ the time resolution in the data

we view $a \to \sigma^2(a)$ , $a \to b(a)$ as unknown $\mathcal{C}^1$ functions and use kernel estimators with kernel $K(\cdot)$ and bandwidth $h > 0$ to plot clouds of points

$$(\, a\,, \widehat{\sigma^2}(a)\,)_{a\in G}\;, \quad (\, a\,, \widehat{b}(a)\,)_{a\in G}\;, \quad \text{for suitable grids } G$$

in order to make appear a typical shape

kernel $K(\cdot)$ : rectangular, triangular, normal ...

using $M$-step $\Delta$-increments in the trajectory for suitable $M$ from H. 07

$$\widehat{\sigma^2}(a) := \widehat{\sigma^2}_{(\Delta,M,h)}(a) = \frac{\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta}-a}{h}\right)\left(\frac{X_{(i+M)\Delta}-X_{i\Delta}}{\sqrt{\Delta\cdot M}}\right)^2}{\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta}-a}{h}\right)}$$

$$\widehat{b}(a) := \widehat{b}_{(\Delta,M,h)}(a) = \frac{\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta}-a}{h}\right)\left(\frac{X_{(i+M)\Delta}-X_{i\Delta}}{\Delta\cdot M}\right)}{\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta}-a}{h}\right)}$$

our choices : bandwith $h = 0.01$, step multiple $M = 20$ (check stability under moderate variation of $M$ and $h$) ; $\Delta$ imposed by structure of data

guideline for estimation of $\sigma^2(\cdot)$ : asymptotics $\widetilde{\Delta} \downarrow 0$ as in Florens-Zmirou 93, Hoffmann 99+01, Jacod 10, .... , for $T_1$ fixed ;

for estimation of $b(\cdot)$ : assuming ergodicity as in Kutoyants 04 ...., continuous observation up to time $T_1$, for $T_1 \to \infty$

have tightness results in terms of an observable random rate involving

$$\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta}-a}{h}\right) \qquad \text{'number of visits near } a\text{'}$$

thus 'estimation is reliable at points $a$ where the number of visits is high'

remark on asymptotics (notation : $T_0 = 0,\ T_1 = T,\ i_0 = 0,\ i_1 = \lfloor \frac{T}{\Delta} \rfloor$) :
if we were free to vary $\Delta$ and $T$, keeping $M$ fixed, then

proposition : a) under the asymptotics

$$(AS1) \qquad T \equiv \text{cst}\ ,\ \text{and}\ \Delta \downarrow 0\ ,\ h \downarrow 0\ ,\ h = o\left(\Delta^{1/3}\right)$$

we have tightness of rescaled estimation errors at observable random rate

$$\sqrt{\sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta} - a}{h}\right)}\ \left(\widehat{\sigma^2}_{(\Delta,M,h)}(a) - \sigma^2(a)\right)$$

b) under ergodicity/stationarity of $(X_t)_{t\geq 0}$ and under asymptotics

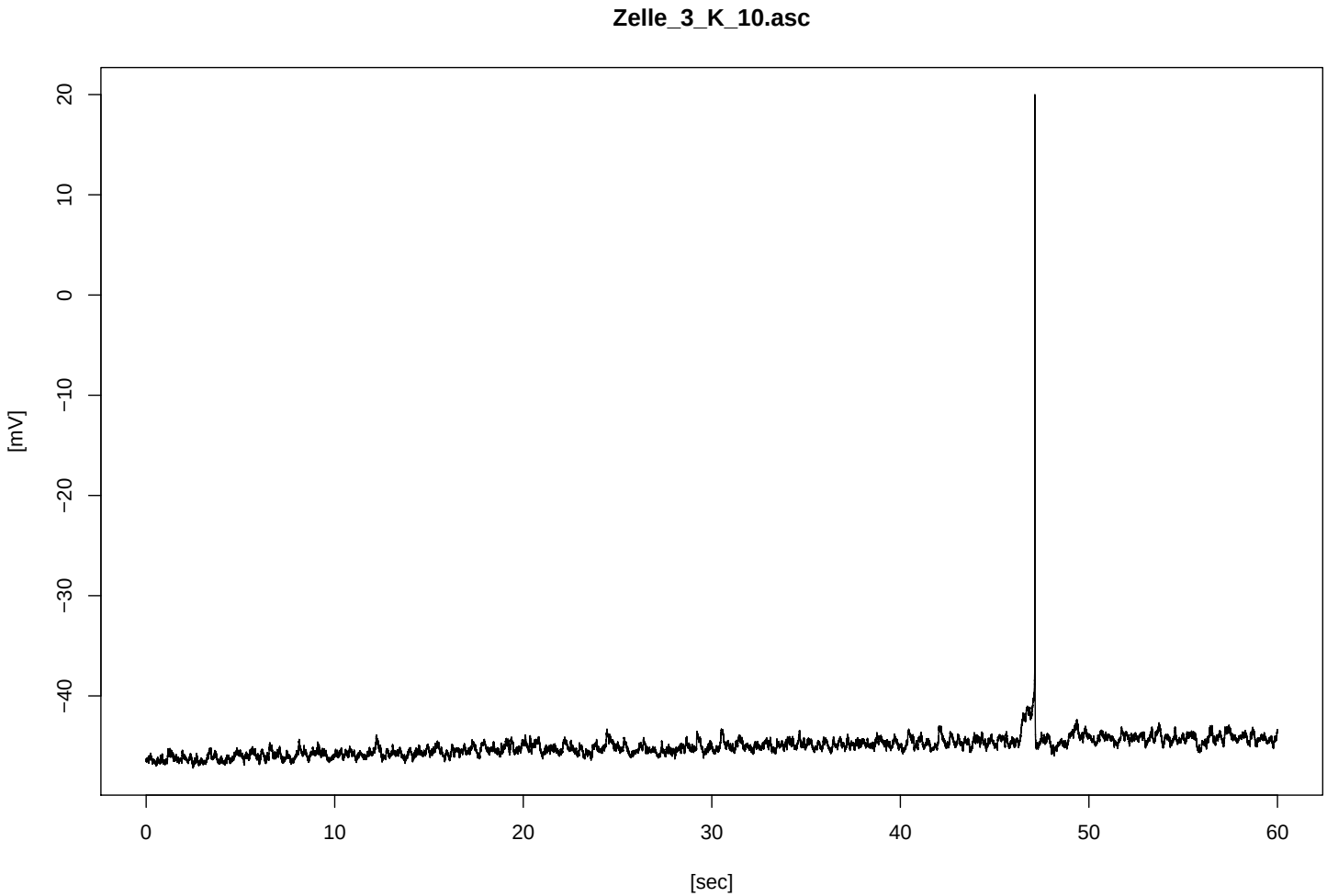
$$(AS2) \qquad \Delta\ \text{small}\ ,\ \text{and}\ T \uparrow \infty\ ,\ h \downarrow 0\ ,\ h = o\left(T^{-1/3}\right)$$

we have tightness of rescaled estimation errors

$$\sqrt{\Delta \cdot \sum_{i=i_0}^{i_1-M} K\left(\frac{X_{i\Delta} - a}{h}\right)}\ \left(\widehat{b}_{(\Delta,M,h)}(a) - b(a)\right)$$

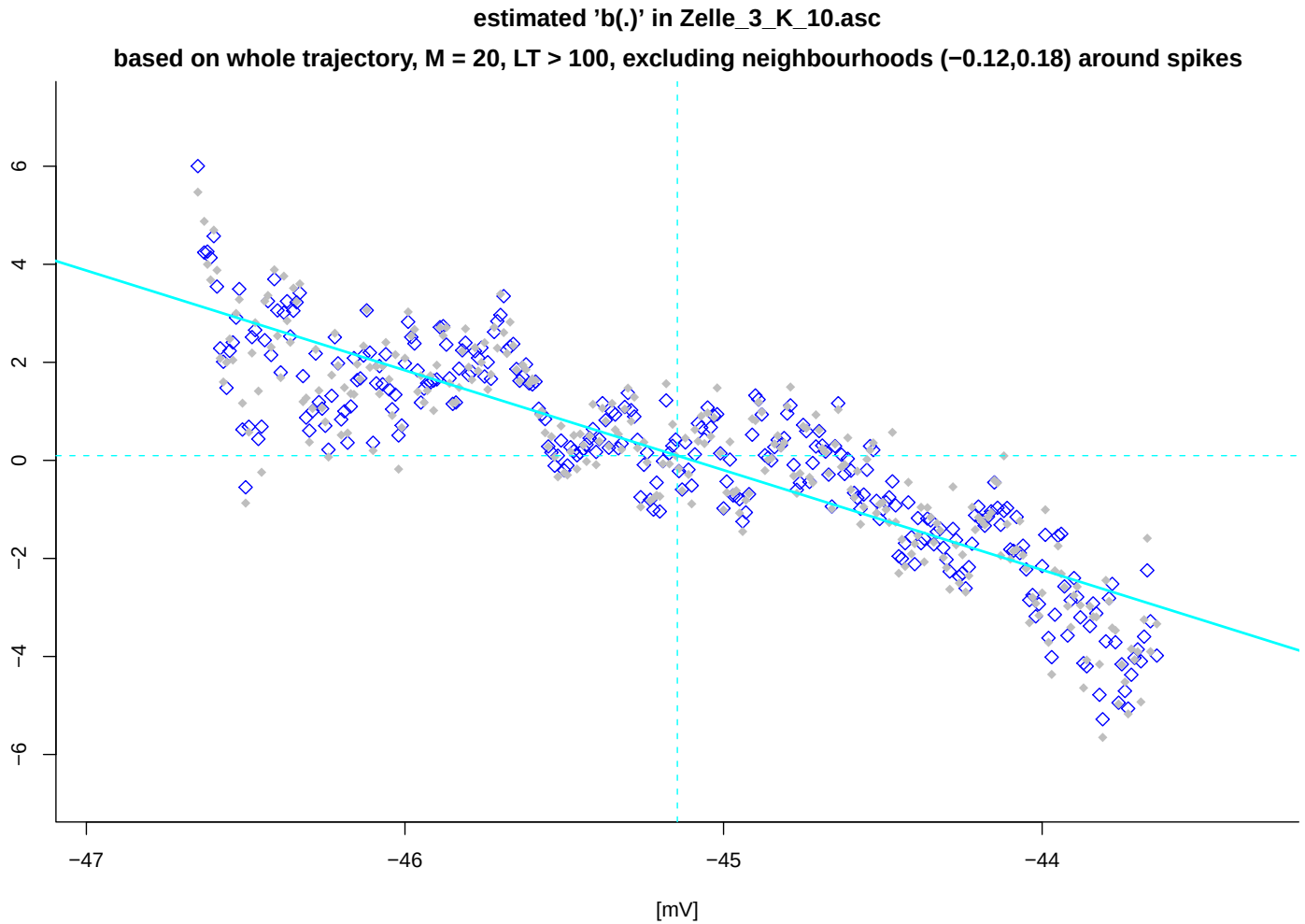
out of the 10 levels in `'Zelle_3'` (potassium bath of varying concentration), we pick the level 8 which has one isolated spike over 60 seconds of observation time (`'Zelle_3_K_10'`), and apply the above estimators to inter-spike-segments in the membrane potential

from H. 07



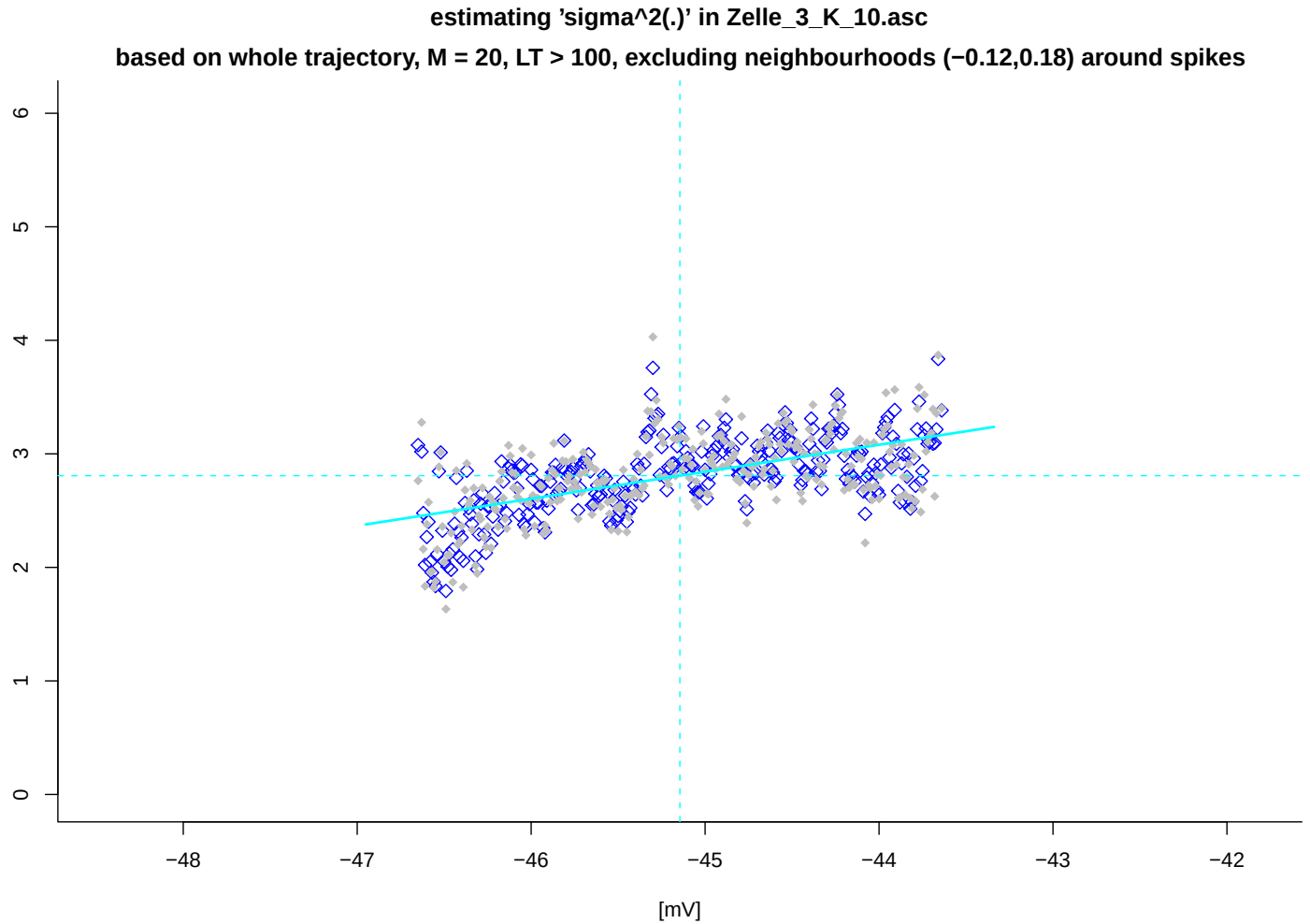

this example : good fit with a CIR type diffusion

drift estimation :




correlation coefficient $= -0.877$, negative slope $= -2.036$

diffusion coefficient estimation :




correlation coefficient $= 0.588$, positive slope $= 0.238$

similiarly, we can see OU type or P type drift and diffusion cofficient in the non-spiking levels 1–7 in example 2

*simulated diffusion equivalent* : any simulated diffusion path using estimated drift and estimated diffusion coefficient ;
for our data `'17Sept08_023'` and for most levels of `'Zelle_3'`,
pictures as seen above can be reproduced from simulated diffusion equivalents

but we do have a number of problems with `'Zelle_3'` :

- some levels might have jumps, in which case we estimate not drift and diffusion coefficient itself, but (drift + associated jump terms) and (diffusion coefficient + associated jump terms)
- strong time inhomogeneities do exist in some levels (e.g. obviously in 1, 2, 4), 'recent past variants' of kernel estimators as above make them appear
- in the spiking level 10 (15 mM of K, 8 spikes) of `'Zelle_3'`, changing $M = 10, 20, 40$ sensibly affects estimation of the diffusion cofficient

## to which extent is the membrane potential between successive spikes adequately modelled as a (continous) semimartingale ?

model assumption : i) the membrane potential between successive spikes (i.e. on suitable intervals $[T_0, T_1]$ sufficiently away from the spike times) is an Ito semimartingale as in Ait-Sahalia and Jacod AS 2009

$$dX_t = b_t\,dt + \sigma_t\,dW_t + \int \kappa \circ \delta(t,y)\,(\mu-\nu)(dt,dy) + \int \kappa' \circ \delta(t,y)\,\mu(dt,dy)$$

(processes $b$, $\sigma$, $\delta$, truncation functions $\kappa(y) = y1_{\{|y|\leq 1\}}$, $\kappa'(y) = y1_{\{|y|>1\}}$)
ii) data : discrete observation of $X$ at time resolution $\Delta$

$$X_{i\Delta}\ ,\ i_0 \leq i \leq i_1\ ,\quad i_0 := \lceil \frac{T_0}{\Delta} \rceil\ ,\ i_1 := \lfloor \frac{T_1}{\Delta} \rfloor$$

aim : apply 'test for jumps' in Ait-Sahalia and Jacod AS 2009 to data and ask

- can the data be viewed as a continuous semimartingale ?
- can the data be viewed as a semimartingale having jumps ?

and finally –the test by Ait-Sahalia and Jacod establishing a dichotomy– ask

- can we assume a semimartingale model for our membrane potential data ?

there will be a surprising answer ...

consider $T_0 = 0$, $T_1 = T$, and also $0 \leq S < T$ ; on $]]S, T]]$ :

if we were free to work with arbitrary $\widetilde{\Delta} \downarrow 0$, we would use usual $p$-variations

$$\widehat{B}_{S,T}(p, \widetilde{\Delta}) := \sum_{i=1}^{\lfloor (T-S)/\widetilde{\Delta} \rfloor} \left| X_{S+i\widetilde{\Delta}} - X_{S+(i-1)\widetilde{\Delta}} \right|^p \quad \text{as} \quad \widetilde{\Delta} \downarrow 0$$

defined w.r.t. non-intersecting intervals (work of Jacod, Barndorff-Nielsen, ...) ; in order to isolate Gaussian parts as $\widetilde{\Delta} \downarrow 0$, we would use truncated $p$-variations

$$\check{B}^{\epsilon}_{S,T}(p, \widetilde{\Delta}) := \sum_{i=1}^{\lfloor (T-S)/\widetilde{\Delta} \rfloor} 1_{\left\{ \left| X_{S+i\widetilde{\Delta}} - X_{S+(i-1)\widetilde{\Delta}} \right| < [\widetilde{\Delta}]^{\frac{1-\epsilon}{2}} \right\}} \left| X_{S+i\widetilde{\Delta}} - X_{S+(i-1)\widetilde{\Delta}} \right|^p$$

motivated by LIL (Mancini SJS '09, SPA '10, Podolskii and Ziggel SISP '10)

in our data, it is impossible to make work convergence results of this type ... can only mimick $\widetilde{\Delta} \downarrow 0$ in a very poor way by considering

$$\widetilde{\Delta} := M\Delta \quad , \quad M = \ldots, 5, 4, 3, 2, 1$$

decreasing multiples of the step size $\Delta$ prescribed by the data

for $T_0 = 0,\ T_1 = T$ and step size $\Delta$ in the data, write $i_0 = 0,\ i_1 = \lfloor \frac{T}{\Delta} \rfloor$

for varying $M$ and $p$, we will use $M$-step $\Delta$-increments in the trajectory, and will mix $p$-variations as above

$$V_{0,T,\infty}(p,\Delta,M) \ := \ \frac{1}{M}\sum_{\ell=0}^{M-1} \widehat{B}_{\ell\Delta,T}(p,M\Delta) \ = \ \frac{1}{M}\sum_{i=i_0}^{i_1-M} \left|X_{(i+M)\Delta} - X_{i\Delta}\right|^p$$

and work with overlapping intervals ; the $M$ summands in the second term being 'almost identical', we identify (heuristics !)

$$V_{0,T,\infty}(p,\Delta,M) \ \approx \ \widehat{B}_{0,T}(p,M\Delta)$$

then transfer established convergence results for $\widehat{B}_{0,T}(p,\widetilde{\Delta})$ as $\widetilde{\Delta} \downarrow 0$ to $V_{0,T,\infty}(p,\Delta,M)$ for decreasing $M = \ldots, 3, 2, 1$

our truncated $p$-variations will be (Höpfner 10)

$$V_{0,T,Z}(p,\Delta,M) \ := \ \frac{1}{M}\sum_{i=i_0}^{i_1-M} 1_{\left\{ \left|X_{(i+M)\Delta}-X_{i\Delta}\right| < 3\cdot[M\Delta]^{\frac{1}{2}}\cdot Z \right\}} \left|X_{(i+M)\Delta} - X_{i\Delta}\right|^p$$

where we play around with the deterministic truncation factor $Z,\ Z \uparrow \infty$

in spiking neurons : several disjoint diffusion-like segments : we add up the corresponding terms coming from the segments

# varying multiples $M$ of $\Delta$ when $p = 2, 4$ is fixed

on the basis of the above heuristics consider 2- and 4-variations :

4-variations : the test for jumps in Ait-Sahalia and Jacod AS 2009

$$\begin{cases} X \text{ with jumps :} & \widehat{B}_{0,T}(4,\widetilde{\Delta}) \overset{\widetilde{\Delta}\downarrow 0}{\longrightarrow} & \sum_{0<s\leq T} |X_s - X_{s-}|^4 & \text{(str. pos. limit)} \\ X \text{ continous :} & \widehat{B}_{0,T}(4,\widetilde{\Delta}) \overset{\widetilde{\Delta}\downarrow 0}{\sim} & \widetilde{\Delta} \cdot \left[ m_4 \int_0^T \sigma_s^4 ds \right] & \text{(linearity in } \widetilde{\Delta}) \end{cases}$$

should be rephrased in our setting as follows : while decreasing $M = \ldots, 3, 2, 1$,

$$\begin{cases} X \text{ with jumps :} & V_{0,T,\infty}(4,\Delta,M) \text{ stabilizes at a strictly positive 'limit'} \\ X \text{ continous :} & V_{0,T,\infty}(4,\Delta,M) \text{ is approx. linear in } M, \text{ and null at 0} \end{cases}$$

2-variations : the well known convergence

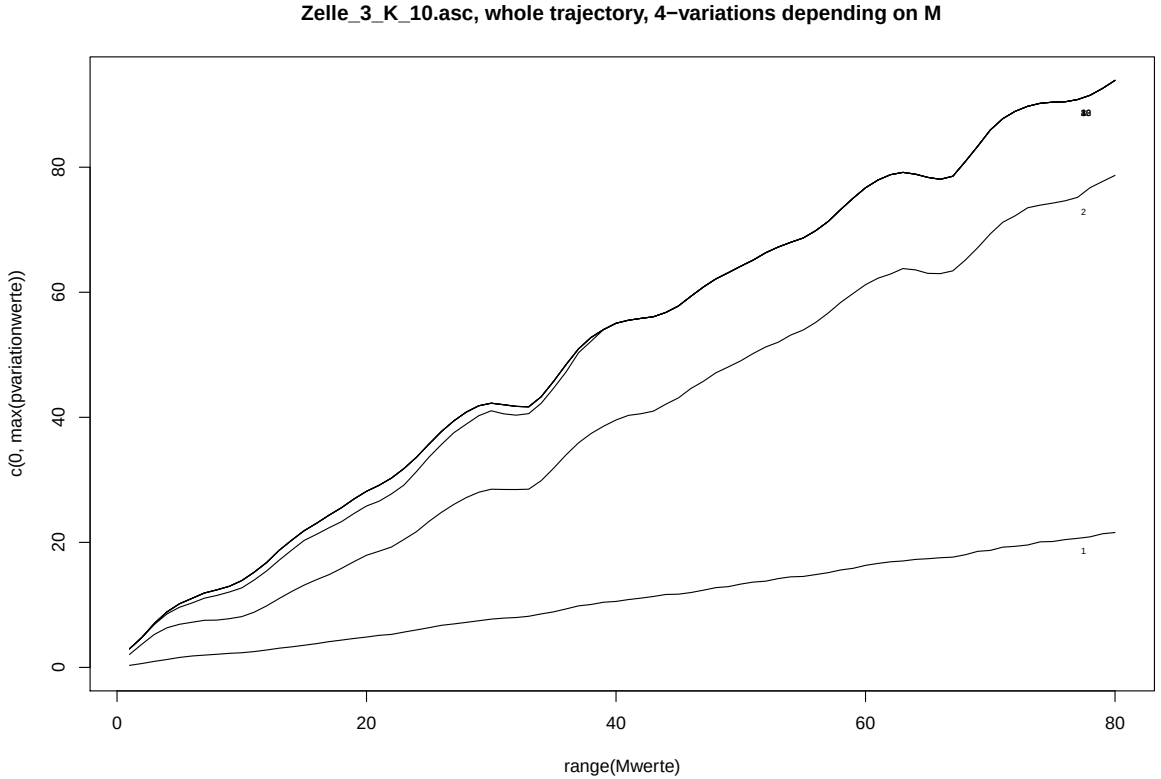
$$\widehat{B}_{0,T}(2,\widetilde{\Delta}) \overset{\widetilde{\Delta}\downarrow 0}{\longrightarrow} [X,X]_T = \int_0^T \sigma_s^2 ds + \sum_{0<s\leq T} |X_s - X_{s-}|^2$$

should translate as follows : for decreasing and sufficiently small values of $M$,

$$V_{0,T,\infty}(2,\Delta,M) \text{ is strictly positive and flat in } M$$

## non- or very rarely spiking neurons : 4-variations as a function of $M$

data `'Zelle_3_K_10'` (level 8), one isolated spike over 60 seconds :

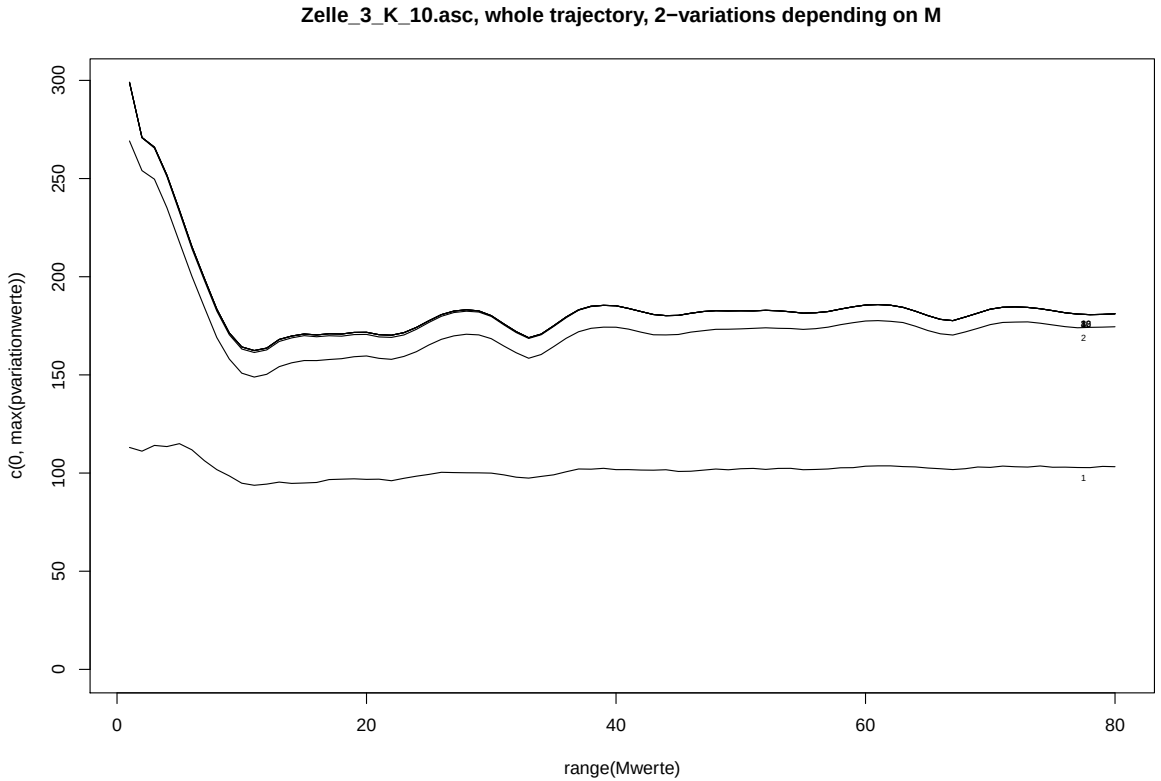



good linearity for all $Z \in \{1, 2, 4, 8, 10, 16, 32, \ldots\}$, no changes above $Z \geq 8$
periodic deformations (circuits/loops in the neuronal slice ?)
no clear hint to presence of jumps : behaviour of a (continuous) semimartingale

similiar pictures for all non-spiking levels 1–7 of `'Zelle_3'`

## non- or very rarely spiking neurons : 2-variations as a function of $M$

same data 'Zelle_3_K_10', level 8 , one isolated spike :



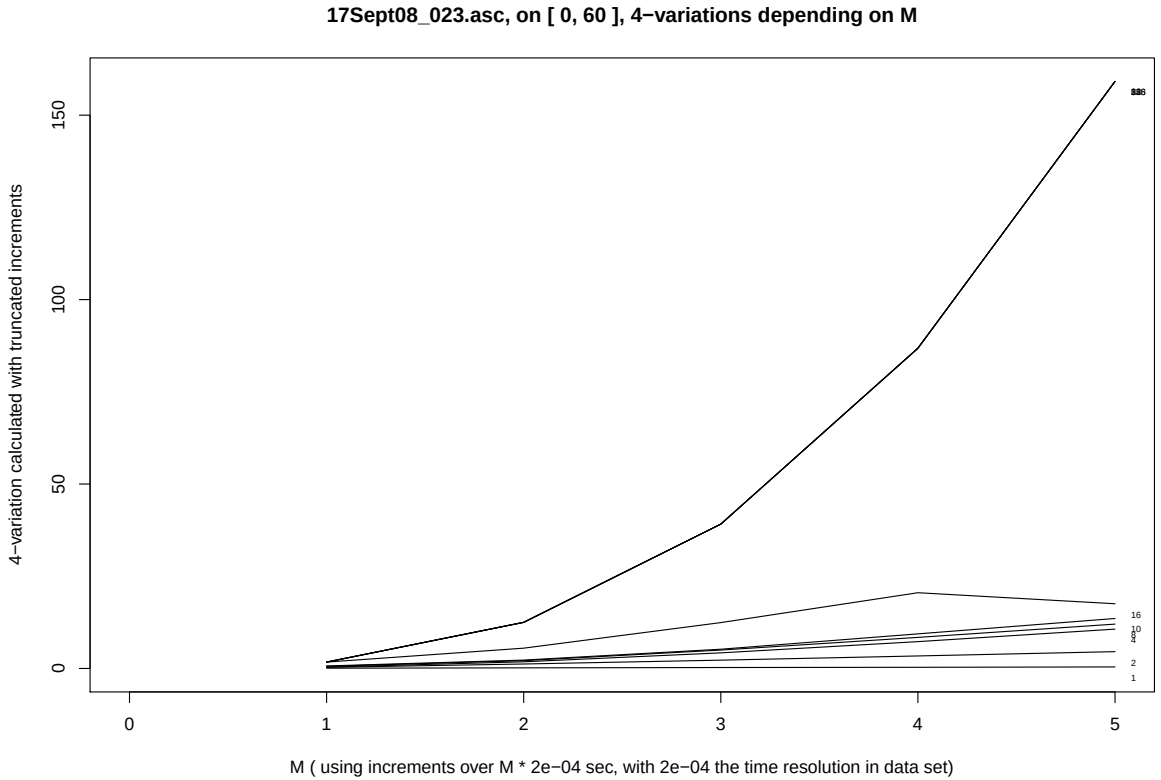

essentially flat in $M$ for $M \geq 15$, for all values of truncation factor $Z$
same periodic deformations observable as above (circuits ?)
'microstructure noise' visible for small $M$, probably due the recording electrode
(similiar in all levels of 'Zelle_3', not present in '17Sept08_023')

behaviour of a semimartingale, up to noisy observation
similiar pictures for all non-spiking levels 1–7 of 'Zelle_3'

## sufficiently frequently spiking neurons : 4-variations as a function of $M$

in a semimartingale, for $p = 4$ fixed and $M = \ldots, 3, 2, 1$ decreasing, 4-variations should be either linear or converging to a strictly positive limit

inspecting the frequently spiking neuron '17Sept08_023' ($\approx 50$ spikes over 60 seconds, no 'noise'), we see none of both : semimartingale property violated

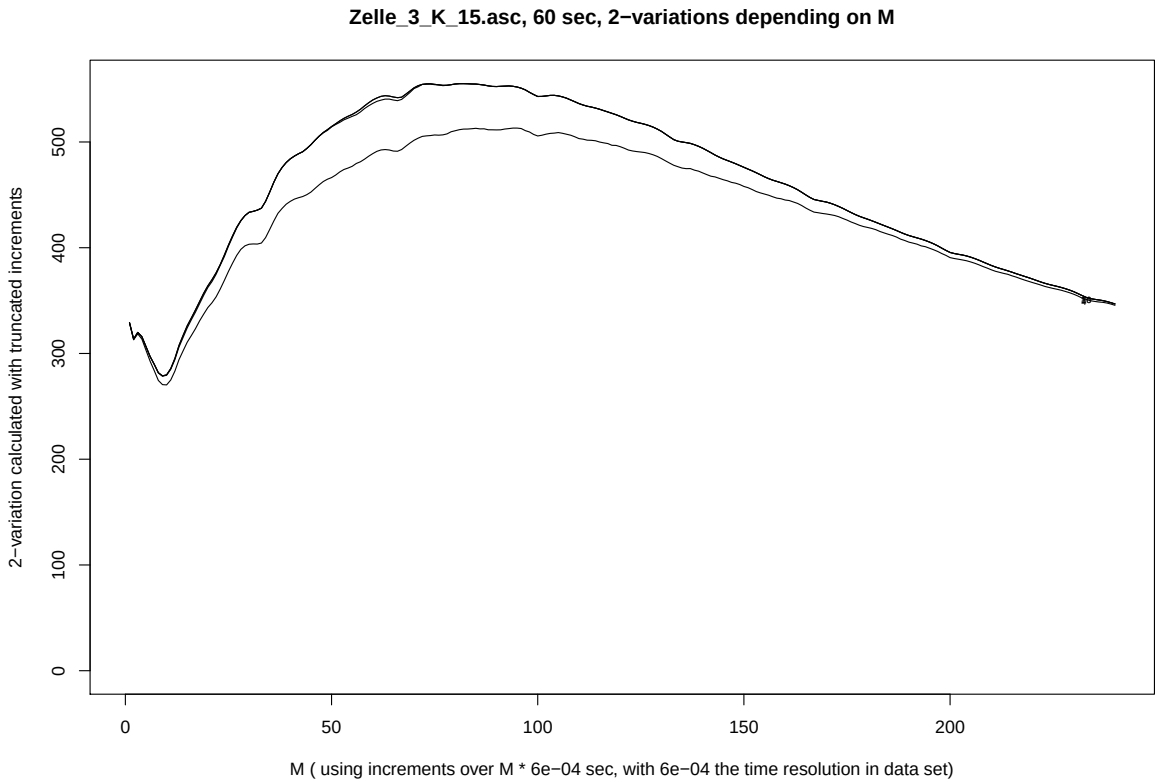



(truncation factors $Z \in \{1, 2, 4, 8, 10, 16, 32, 64, \ldots\}$, no changes for $Z \geq 32$)

## sufficiently frequently spiking neurons : 2-variations as a function of $M$

in a semimartingale, for $p = 2$ fixed and $M = \ldots, 3, 2, 1$ decreasing, 2-variations should be flat in $M$

for the spiking level 10 (`'Zelle_3_K_15'`, 8 spikes over 60 seconds), we see




(truncation factors as above, noisy observation visible in small $M$-values)

semimartingale property violated : similiar pictures also for level 9 of `'Zelle_3'` (18 spikes), and for `'17Sept08_023'`

# varying $p$ when the multiple $M$ of $\Delta$ is fixed

the test for jumps in Ait-Sahalia and Jacod AS 09

$$\begin{cases} \text{for } \xi \text{ with jumps} : & \widehat{B}_{0,T}(p, 2\widetilde{\Delta}) \approx \begin{cases} \widehat{B}_{0,T}(p, \widetilde{\Delta}) & \text{for } 2 \leq p < \infty \\ 2^{\frac{p}{2}-1}\, \widehat{B}_{0,T}(p, \widetilde{\Delta}) & \text{for } 0 < p < 2 \end{cases} \\ \text{for } \xi \text{ continuous} : & \widehat{B}_{0,T}(p, 2\widetilde{\Delta}) \approx 2^{\frac{p}{2}-1}\, \widehat{B}_{0,T}(p, \widetilde{\Delta}) \quad \text{for } 0 < p < \infty \end{cases}$$

(for $\widetilde{\Delta}$ small enough) translates in our setting as follows : empirical log-ratios

$$p \longrightarrow \log \frac{V_{0,T,\infty}(p, \Delta, 2M)}{V_{0,T,\infty}(p, \Delta, M)} \approx \log \frac{\widehat{B}_{0,T}(p, 2M\Delta)}{\widehat{B}_{0,T}(p, M\Delta)}$$

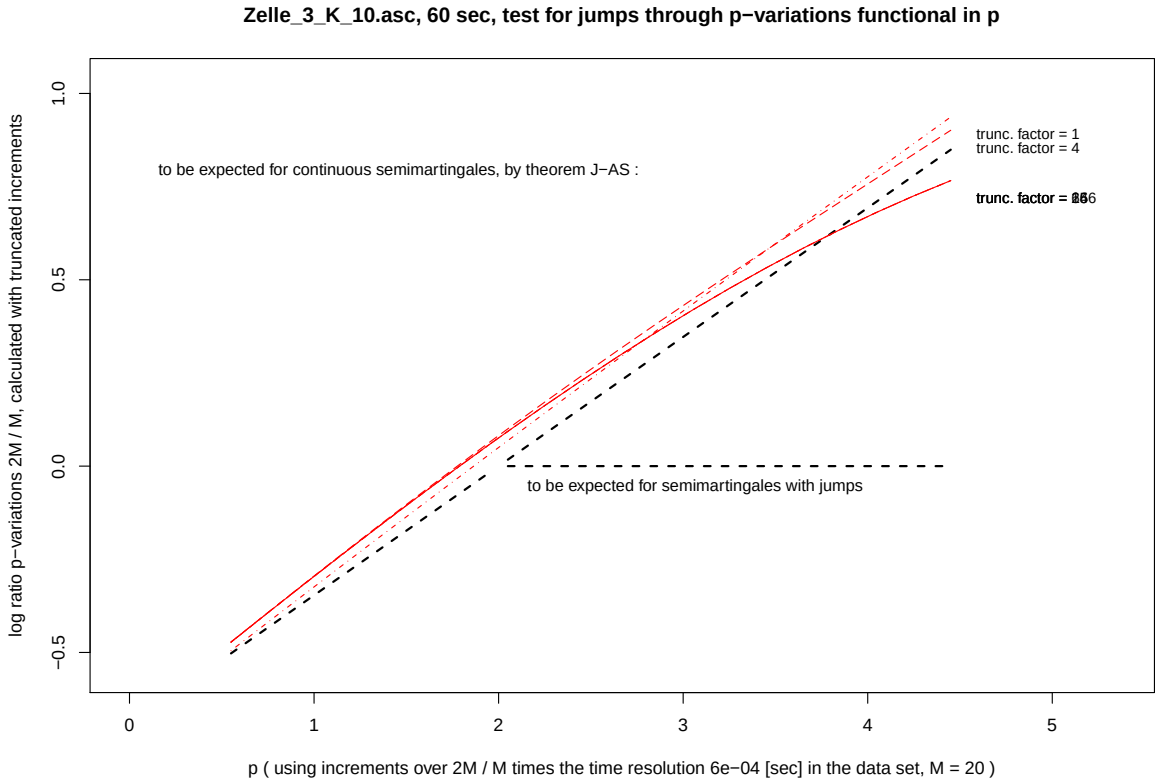
(heuristics as above !) should be close to the deterministic function

$$\begin{cases} p \to \min\left\{(\frac{p}{2} - 1)\log 2\,,\, 0\right\} & \text{on } \ 0 < p < \infty \quad \text{if } \xi \text{ has jumps} \\ p \to (\frac{p}{2} - 1)\log 2 & \text{on } \ 0 < p < \infty \quad \text{if } \xi \text{ is continuous} \end{cases}$$

in our data, we work again with $M = 20$

## non- or very rarely spiking neurons : empirical log-ratios as a function of $p$

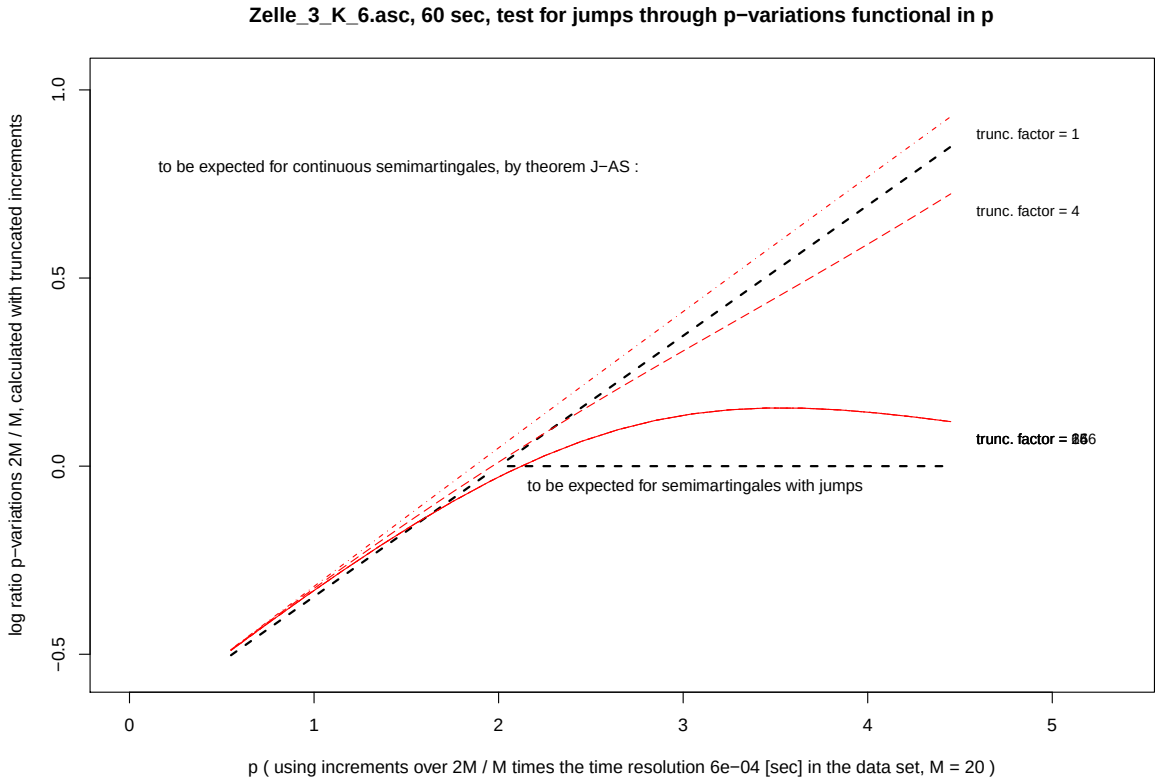
data 'Zelle_3_K_10', level 8, one isolated spike :




(truncation factors $Z \in \{1, 4, 16, 64, 256\}$, no changes above $Z \geq 16$)

essentially linear in $p$ : behaviour of a continuous semimartingale
up to two exceptions, the non-spiking levels 1–7 produce this type of picture

among the non-spiking levels 1–7 of 'Zelle_3', the present methods detects jumps in some cases : here level 4 ('Zelle_3_K_6'), truncation fact. as above :

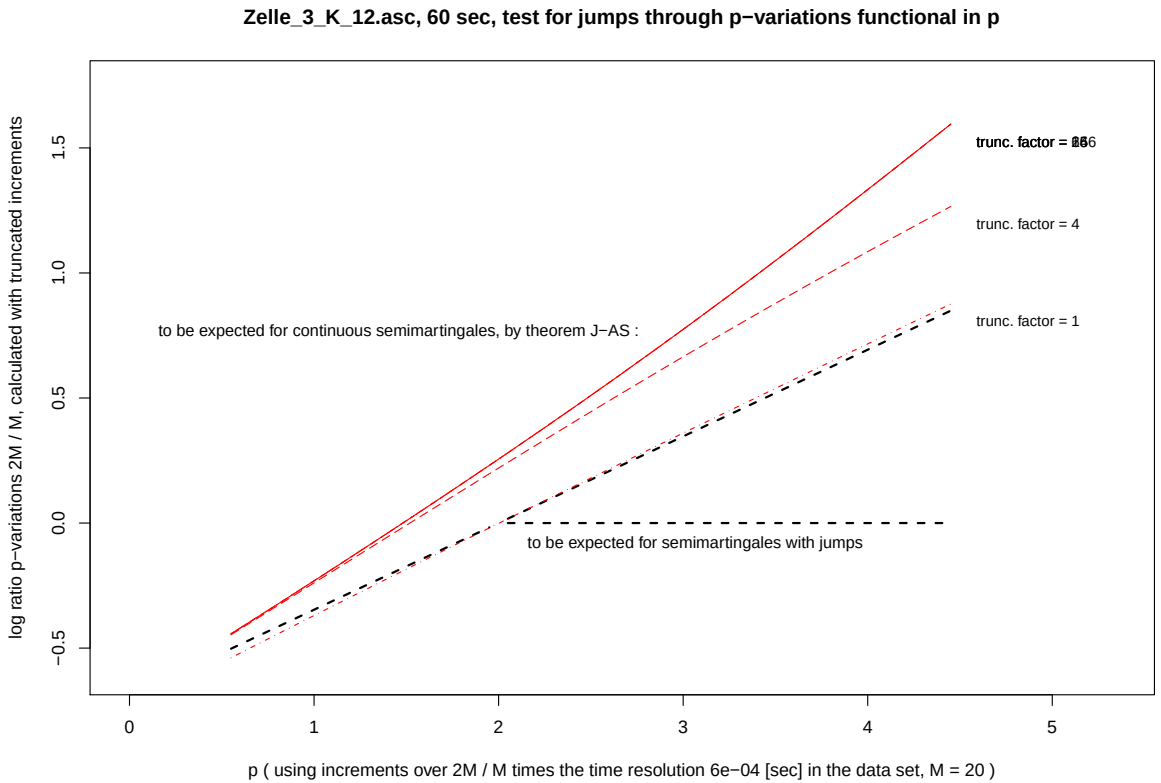



behaviour of a semimartingale with jumps

so far : can conclude from our data : in non-spiking or very rarely spiking regimes, the membrane potential is adequately modelled as a semimartingale, in some cases with jumps

## sufficiently frequently spiking neurons : empirical log-ratios as a function of $p$

in a semimartingale, for $M$ fixed and varying $p$, empirical log-ratios should be either linear in $p$ (with known slope), or linear with truncation at 0 for $p \geq 2$ ; in `'Zelle_3_K_12'`, level 9, 18 spikes, none of both :




(truncation factors $Z \in \{1, 4, 16, 64, 256\}$, no changes above $Z \geq 16$)

semimartingale property violated ;
similiar pictures for level 10 of `'Zelle_3'` (8 spikes), and for `'17Sept08_023'`

# the disturbing conclusion

frequently spiking neuron '17Sept08_023', spiking levels 9+10 of 'Zelle_3' : power variations calculated from data do not fit into the dichotomy established by Jacod's test for jumps for Ito semimartingales :

hence the membr. pot. between successive jumps in frequently spiking neurons

IS NOT ADEQUATELY MODELLED BY A SEMIMARTINGALE ...

this forbids any semimartingale based approach to 'information transmission' in neurons ... and destroys a large number of papers analyzing interspike times in terms of level crossing times of diffusions

whereas in the non-spiking regimes of levels 1-7 of 'Zelle_3', and even in level 8 where one isolated spike occurs, our data (up to effects of 'noise')

VALIDATE THE SEMIMARTINGALE HYPOTHESIS.

Hence there is a strong need for neuron models which allow to understand non-spiking and spiking regimes simultaneously ...

mathematical :

AitSahalia-Jacod 09 : Testing for jumps in a discretely observed process. AS 37, 184–222 (2009).

Cremers-Kadelka 86 : On weak convergence of ... stochastic processes with applications to processes taking paths in $L_p^E$. SPA 21 (1986).

Dawson-Li 06 : Skew convolution semigroups and affine Markov processes. AP 34, 1103–1142 (2006).

FlorensZmirou 93 : On estimating the diffusion coefficient from discrete observations. JAP 30 (1993).

Grinblat 76 : A limit theorem for measurable random processes and its applications. Proc. AMS 61 (1976).

Hoffmann 99 : $L^p$ estimation of the diffusion coefficient. Bernoulli 5 (1999).

Hoffmann 01 : On estimating the diffusion coefficient : parametric versus nonparametric. Ann. IHP PS 37 (2001).

Höpfner 09 : An extension of the Yamada-Watanabe condition for pathwise uniqueness to SDE with jumps. ECP 14, 447-456 (2009).

Höpfner 09b : A time inhomogeneous Cox-Ingersoll-Ross diffusion with jumps. Preprint 2009, arXiv0906.1856

Höpfner-Kutoyants 10 : Estimating discontinuous periodic signals in a time inhomogeneous diffusion. SISP 2010, to appear, arXiv.

Ikeda-Watanabe 89 : Stochastic differential equations and diffusion processes. North Holland/Kodansha 1989.

Kutoyants 03 : Statistical Inference for ergodic diffusion processes. Springer 2003.

Jacod 10 : Statistics and high frequency data. Preprint, SEMSTAT La Manga 2007, to appear 2010.

Jacod-Shiryaev 87 : Limit theorems for stochastic processes. Springer 1987.

Kawazu-Watanabe 71 : Branching processes with immigration and related limit theorems. TPA 16 (1971).

Mancini 09 : Non-parametric threshold estimation for models with stochastic diffusion coefficient and jumps. SJS 36 (2009)

Fu-Li 08 : Stochastic equations of non-negative processes with jumps. Preprint 2008, arXiv.

Podolskii-Ziggel 10 : A new test for jumps in semimartingales ... SISP 13 (2010)

biological :

Brodda-Höpfner 06 : A ... functional central limit theorem for information processing in large systems of neurons. JMB 52 (2006).

Ditlevsen-Lansky 05 : Estimation of the input parameters in the Ornstein-Uhlenbeck neuronal model. Phys. Rev. E 71 (2005).

Ditlevsen-Lansky 06 : Estimation of the input parameters in the Feller neuronal model. Phys. Rev. E 73 (2006).

Giorny-Lansky-Nobile-Ricciardi 88 : Diffusion approximation and first-passage-time problem for a model neuron. Biol. Cybern. 58 (1988).

Höpfner 07 : On a set of data for the membrane potential in a neuron. MBS 207, 275–301 (2007).

Höpfner 10 : To which extent can the membrane potential in a neuron between successive spikes be modelled as a (continuous) semimartingale ? Preprint 2010, arXiv1008.4233

Jahn 09 : Statistical problems related to excitation threshold and reset value in neurons. PhD thesis, Mainz 2009.

Lansky-Lanska 87 : Diffusion approximation ... with synaptic reversal potentials. Biol. Cybern. 56 (1987).

Lansky-Sacerdote 01 : The Ornstein-Uhlenbeck neuronal model with signal-dependent noise. Physics Letters A 285 (2001).

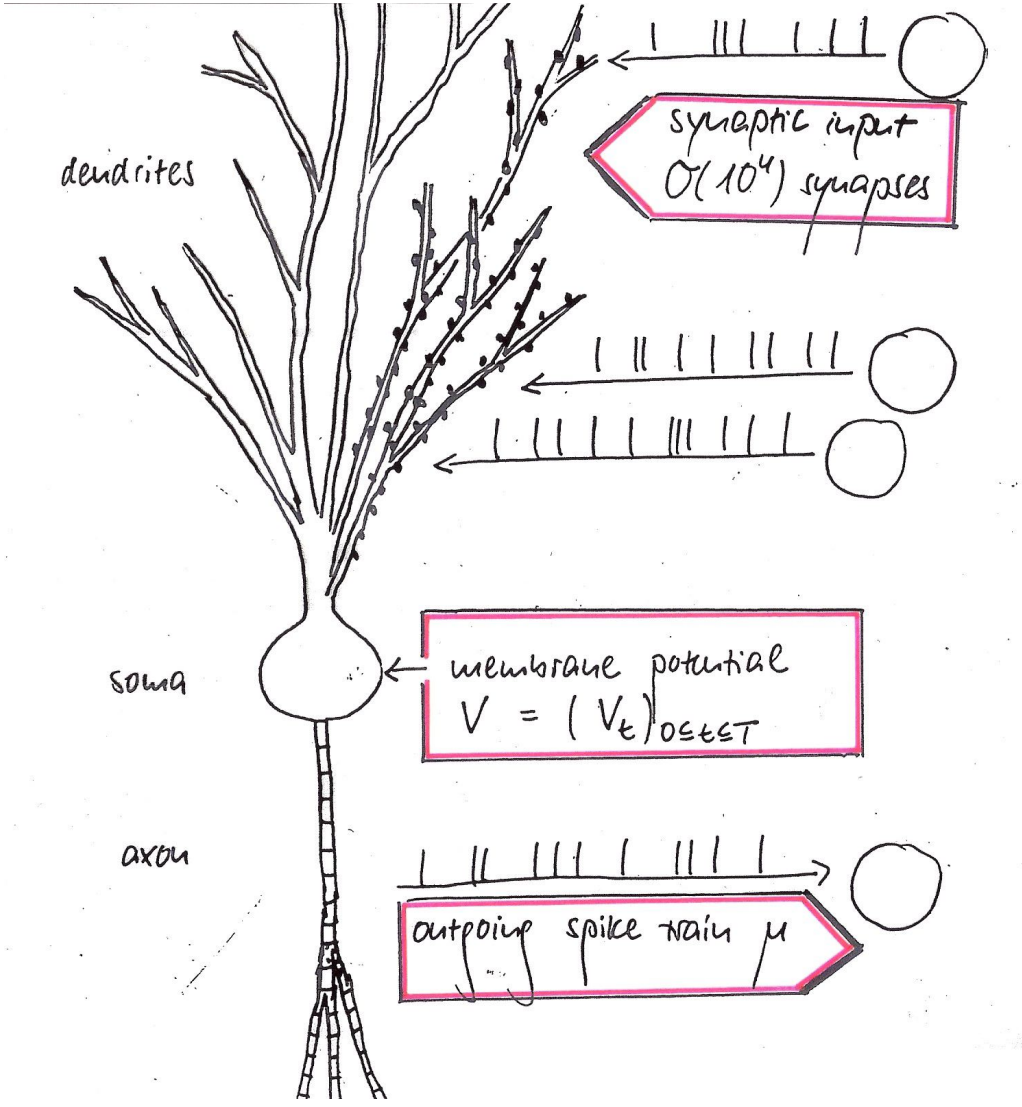
Lansky-Sacerdote-Tomassetti 95 : On the comparison of Feller and Ornstein-Uhlenbeck models ... Biol. Cybern. 73 (1995).

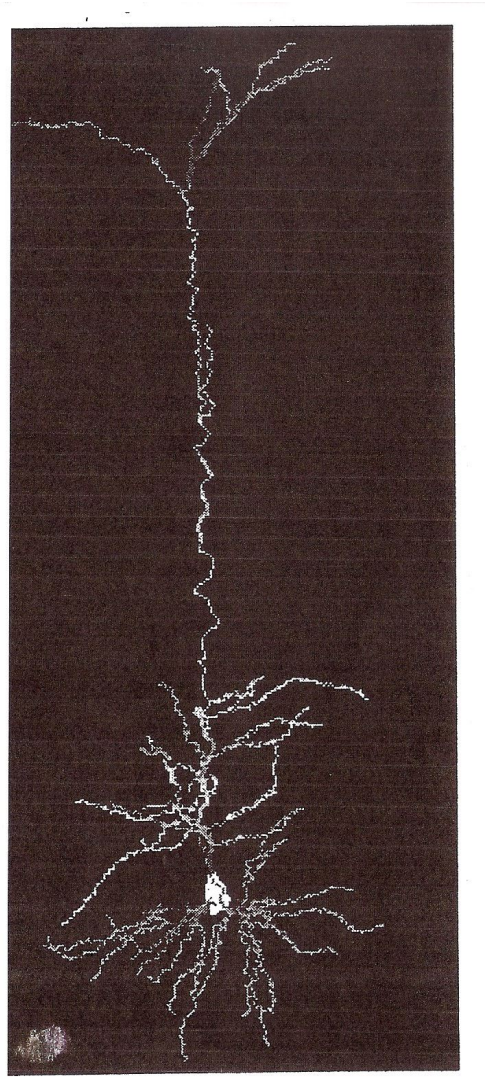
Lansky-Sato 99 : The stochastic diffusion models of ... interspike interval generation. J. Peripheral Nervous System 4 (1999)

Shadlen-Newsome 98 : The variable discharge of cortical neurons. J. Neurosci. **18**, 3870-3896 (1998).

Tuckwell 89 : Stochastic processes in the neurosciences. CBMS-NSF conf. series in applied mathematics, SIAM 1989.

# appendix

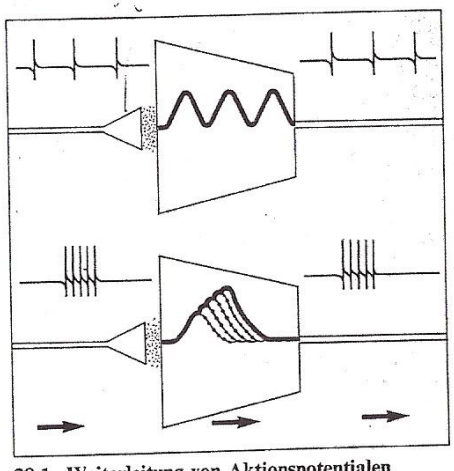


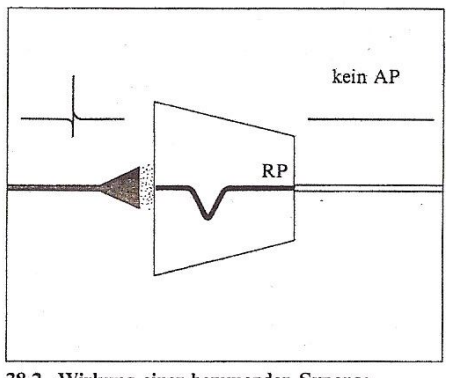
spikes are generated when the membran potential $V_t$ in the soma is high enough

heuristics : why should the membrane potential between successive spikes be modelled as a (jump) diffusion process ?

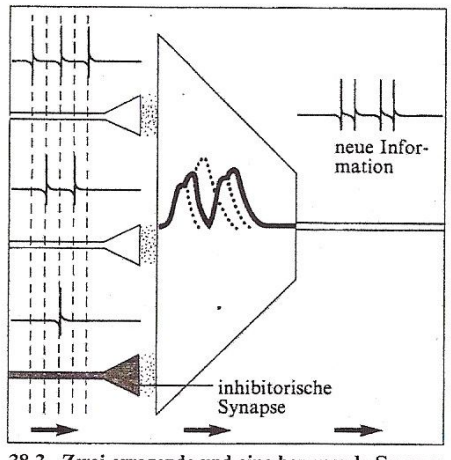
one neuron has $O(10^4)$ synapses, $\approx 90\%$ excitatory, $\approx 10\%$ inhibitory



38.1. Weiterleitung von Aktionspotentialen




38.2. Wirkung einer hemmenden Synapse




38.3. Zwei erregende und eine hemmende Synapse wirken zusammen

contribution of incoming spikes to the membrane potential via : exciting synapsis (L), inhibitory synapsis (M), exciting and inhibitory combined (R)

synapses $\hookrightarrow$ dendrites $\hookrightarrow$ soma : additivity and exponential decay