

Supplement to the article “Extending Cable Theory to Heterogeneous Dendrites” by Claude Meunier and Boris Lamotte dIncamps, *Neural Computation*, Volume 20, Issue 7 (July 2008), pp. 1732-1775.

A Appendices

A.1 Dependence of the voltage on the small scale distribution of synapses

The activation of discrete excitatory synapses on a passive dendrite induce small scale voltage fluctuations, whose variations in space are given by the function $\int \int \delta g_e$, i.e. the second integral of conductance fluctuations (see Section 2). Similarly, the discreteness of synapses introduces a corrective term proportional to $\langle (\int \delta g_e)^2 \rangle$ in the equation governing the evolution of the average voltage. These two quantities depend on the statistical distribution of synapses. They are computed here for three distributions: periodic, periodic perturbed by a random jitter, and random with uniform probability density. In all three case, we consider that the dendrite is a finite length cylinder, and we assume that the synaptic density is uniform in average over the dendrite.

For a periodic distribution of point synapses, the synaptic conductance per unit length reads

$$g_e^{per}(y) = \langle g_e \rangle \lambda \sum_{k=1}^N \delta(y - k\lambda) \quad (A1)$$

in y variable. Subtracting the average $\langle g_e \rangle$ and integrating, we obtain the periodic sawtooth function $\int \delta g_e^{per}(y) = \langle g_e \rangle (\lambda/2 - y)$ (for $0 \leq y \leq \lambda$). We have $\langle (\int \delta g_e)^2 \rangle = \langle g_e \rangle^2 \lambda^2/12$, so that, at steady-state,

$$\langle V_2 \rangle = - \left(\frac{\langle g_e \rangle}{\langle g_e \rangle + g_m} \right)^2 \frac{V_e}{12} \quad (A2)$$

Integrating again, we obtain the periodic function $\int \int \delta g_e^{per}(y)$ equal to $\langle g_e \rangle (-y^2/2 + \lambda y/2 - \lambda^2/12)$ on $[0, \lambda]$.

When a jitter ξ_k , $1 \leq k < N$ is added, the synaptic conductance becomes $g_e(y) = \langle g_e \rangle \lambda \sum_{k=1}^N \delta(y - y_k)$,

where $y_k = k\lambda + \xi_k\lambda$ is the position of the k -th synapse. It follows that

$$\delta g_e(y) = \delta g_e^{per}(y) + \langle g_e \rangle \lambda \sum_{k=1}^N (\delta(y - y_k) - \delta(y - k\lambda))$$

where $g_e^{per}(y)$ denotes the synaptic conductance in the absence of jitter. We have then

$$\int \delta g_e(y) = \int \delta g_e^{per}(y) + \langle g_e \rangle \lambda \left(\sum_{k=1}^N \chi_k(y) + \frac{1}{N} \sum_{k=1}^N \xi_k \right) \quad (\text{A3})$$

where the function $\chi_k(y) = \Theta(y - y_k) - \Theta(y - k\lambda)$ is the difference of two Heaviside step functions, with jumps at $k\lambda$ and y_k respectively, and has for spatial average $-\xi_k/N$. Using the identities $\langle \chi_k(y)^2 \rangle = |\xi_k|/N$, and $\langle \int \delta g_e^{per}(y) \chi_k(y) \rangle = \langle g_e \rangle \lambda (\xi_k^2 - \xi_k)/2N$, one obtains

$$\left\langle \left(\int \delta g_e \right)^2 \right\rangle = \left\langle \left(\int \delta g_e^{per} \right)^2 \right\rangle + \langle g_e \rangle^2 \lambda^2 \left(-\frac{1}{N} \sum_{k=1}^N \xi_k + \frac{1}{N} \sum_{k=1}^N |\xi_k| + \frac{1}{N} \sum_{k=1}^N \xi_k^2 - \frac{1}{N^2} \left(\sum_{k=0}^N \xi_k \right)^2 \right)$$

The expectation of $\left\langle \left(\int \delta g_e \right)^2 \right\rangle$ is equal to $\left\langle \left(\int \delta g_e^{per} \right)^2 \right\rangle + \langle g_e \rangle^2 \lambda^2 (E[|\xi|] + (1 - 1/N)Var[\xi])$. Its variance is $(\langle g_e \rangle^4 \lambda^4 / N) (Var[\xi] + Var[|\xi|] + (1 - 1/N)^2 Var[\xi^2] + 2(1 - 1/N)(E[|\xi|\xi^2] - E[|\xi|]E[\xi^2] + E[\xi^2]^2 / N))$. It goes to 0 as N goes to infinity.

To estimate the error made when neglecting small scale voltage fluctuations, we must calculate the expectation and variance of $\iint \delta g_e$. We have

$$\begin{aligned} \iint \delta g_e(y) &= \iint \delta g_e^{per}(y) + \langle g_e \rangle \lambda \sum_{k=1}^N \chi_k(y) (y - y_k) + \langle g_e \rangle \lambda^2 \left(\frac{y}{N\lambda} - \frac{1}{2} \right) \sum_{k=1}^N \xi_k \\ &\quad - \langle g_e \rangle \lambda^2 \sum_{k=1}^N \xi_k \left(\theta(y - k\lambda) + \frac{k}{N} - 1 \right) - \frac{\langle g_e \rangle \lambda^2}{2N} \sum_{k=1}^N \xi_k^2 \end{aligned} \quad (\text{A4})$$

The expectation of $\iint \delta g_e(y)$ is the periodic function of y with zero spatial average

$$E \left[\iint \delta g_e(y) \right] = \iint \delta g_e^{per}(y) - \frac{\langle g_e \rangle \lambda^2}{2} Var[\xi] + \langle g_e \rangle \lambda \sum_{k=1}^N (E[(y - y_k)\theta(y - y_k)] - (y - k\lambda)\theta(y - k\lambda))$$

The variance of $\iint \delta g_e(y)$ is also a periodic function of y . However, it becomes independent of y in the large

N limit and is then equal to $N \langle g_e \rangle^2 \lambda^4 \text{Var}[\xi]/12$.

If the random variables ξ_k are uniformly drawn in $[-\xi_{max}, \xi_{max}]$ (with $0 \leq \xi_{max} \leq 1/2$ to avoid swapping adjacent synapses), we can compute explicitly the previous quantities. In the large N limit, we obtain

$$\begin{aligned} E \left[\left\langle \left(\int \delta g_e \right)^2 \right\rangle \right] &= \left\langle \left(\int \delta g_e^{per} \right)^2 \right\rangle (1 + 6\xi_{max} + 4\xi_{max}^2) \\ \text{Var} \left(\left\langle \left(\int \delta g_e \right)^2 \right\rangle \right) &= \frac{\langle g_e \rangle^4 \lambda^4}{N} (2\xi_{max}^2/3 + 2\xi_{max}^3/6 + \xi_{max}^4/5) \\ E \left[\iint \delta g_e(y) \right] &= \iint \delta g_e^{per}(y) + \frac{\langle g_e \rangle}{4\xi_{max}} (\xi_{max}\lambda - z\lambda)^2 \theta(\xi_{max}\lambda - z\lambda) - \frac{\langle g_e \rangle \lambda^2 \xi_{max}^2}{6} \\ \text{Var} \left(\iint \delta g_e(y) \right) &= \frac{N \langle g_e \rangle^2 \lambda^4 \xi_{max}^2}{36} \end{aligned}$$

where $z\lambda = \min(|y - j\lambda|)$ ($1 \leq j \leq N$) is the distance from location y to the closest $j\lambda$.

These quantities are also easily computed when the jitter takes binary values ($\xi_k = \pm\xi_{max}$). One has then

$$\begin{aligned} E \left[\left\langle \left(\int \delta g_e \right)^2 \right\rangle \right] &= \left\langle \left(\int \delta g_e^{per} \right)^2 \right\rangle (1 + 12\xi_{max} + 12\xi_{max}^2) \\ \text{Var} \left(\left\langle \left(\int \delta g_e \right)^2 \right\rangle \right) &= \frac{\langle g_e \rangle^4 \lambda^4 \xi_{max}^2}{N} \\ E \left[\iint \delta g_e(y) \right] &= \iint \delta g_e^{per}(y) + \frac{\langle g_e \rangle}{2} (\xi_{max}\lambda - z\lambda) \theta(\xi_{max}\lambda - z\lambda) - \frac{\langle g_e \rangle \lambda^2 \xi_{max}^2}{2} \\ \text{Var} \left(\iint \delta g_e(y) \right) &= \frac{N \langle g_e \rangle^2 \lambda^4 \xi_{max}^2}{12} \end{aligned}$$

for large N .

We now consider synapses that are randomly distributed with uniform probability. We have then $g_e(y) = \langle g_e \rangle \lambda \sum_{k=1}^N \delta(y - y_k)$, the probability that the location y_k of the k -th synapse on the cable be comprised between a and $a + da$ being given by

$$P(a \leq y_k < a + da) = N C_{N-1}^{k-1} \left(\frac{a}{N\lambda} \right)^{k-1} \left(1 - \frac{a}{N\lambda} \right)^{N-k} \frac{da}{N\lambda} \quad (\text{A5})$$

It follows that $E[y_k^n] = (N\lambda)^n N C_{N-1}^{k-1} B(n+k, N-k+1)$, where $B(p, q) = (p-1)!(q-1)!/(p+q-1)!$ is the complete beta function (Abramowitz and Stegun, 1970). We have then

$$E[y_k^n] = (N\lambda)^n \frac{(n+k-1)!}{(k-1)!} \frac{N!}{(N+n)!}$$

which entails that $E[y_k] = Nk\lambda/(N+1)$, $E[y_k^2] = N^2k(k+1)\lambda^2/(N+1)(N+2)$ and $E[y_k^3] = N^3k(k+1)(k+2)\lambda^3/(N+1)(N+2)(N+3)$. Due to their ordering in increasing order, the random variables y_k are correlated. The probability that y_j be comprised between a and $a+da$ and y_k ($j < k$) between b and $b+db$ is given by

$$P(a \leq y_j < a+da, b \leq y_k < b+db) = N(N-1)C_{N-2}^{j-1}C_{N-j-1}^{k-j-1} \left(\frac{a}{N\lambda}\right)^{j-1} \left(\frac{b-a}{N\lambda}\right)^{k-j-1} \left(1 - \frac{b}{N\lambda}\right)^{N-k} \frac{da}{N\lambda} \frac{db}{N\lambda}$$

It follows that $E[y_j^n y_k^p] = N(N-1)C_{N-2}^{j-1}C_{N-j-1}^{k-j-1}(N\lambda)^{n+p}B(j+n, k-j)B(k+n+p, N-k+1) = (N\lambda)^{n+p}N!(j-1+n)!(k-1+n+p)!/(N+n+p)!(j-1)!(k-1+n)!$. In particular, we have, for $j < k$, $E[y_j y_k] = j(k+1)N^2\lambda^2/(N+1)(N+2)$, $E[y_j^2 y_k] = j(j+1)(k+2)N^3\lambda^3/(N+1)(N+2)(N+3)$ and $E[y_j y_k^2] = j(k+1)(k+2)N^3\lambda^3/(N+1)(N+2)(N+3)$. Similarly, one shows that $E[y_i y_j y_k] = i(j+1)(k+2)N^3\lambda^3/(N+1)(N+2)(N+3)$ for $i < j < k$. In contrast, the locations z_k ($1 \leq k \leq N$) of the synapses in their drawing order are independent and equidistributed. They are symmetrically distributed around their mean $N\lambda/2$, with second moment $N^2\lambda^2/3$ and fourth moment $N^3\lambda^3/80$.

Integrating $\delta g_e(y)$, we obtain

$$\int \delta g_e(y) = \langle g_e \rangle \left(\lambda \sum_{k=1}^N \theta(y - y_k) - y \right) - \langle g_e \rangle \left(\frac{N\lambda}{2} - \frac{1}{N} \sum_{k=1}^N y_k \right) \quad (\text{A6})$$

from which we derive

$$\left\langle \left(\int \delta g_e \right)^2 \right\rangle = \langle g_e \rangle^2 \left(\frac{N^2\lambda^2}{12} + (N+1)\lambda \left(\frac{1}{N} \sum_{k=1}^N y_k \right) - \left(\frac{1}{N} \sum_{k=1}^N y_k \right)^2 + \frac{1}{N} \sum_{k=1}^N y_k^2 - 2\frac{\lambda}{N} \sum_{k=1}^N k y_k \right) \quad (\text{A7})$$

We rewrite this equation as

$$\left\langle \left(\int \delta g_e \right)^2 \right\rangle = \langle g_e \rangle^2 \left(\frac{N^2\lambda^2}{12} + (N+1)\lambda \left(\frac{1}{N} \sum_{k=1}^N z_k \right) - \left(\frac{1}{N} \sum_{k=1}^N z_k \right)^2 + \frac{1}{N} \sum_{k=1}^N z_k^2 - 2\lambda S_N \right) \quad (\text{A8})$$

where we have set $S_N = \sum_{k=1}^N ky_k/N$. We have $E[\sum_{k=1}^N z_k/N] = N\lambda/2$, $E[\sum_{k=1}^N z_k^2/N] = N^2\lambda^2/3$ and $E[(\sum_{k=1}^N z_k/N)^2] = N(3N+1)\lambda^2/12$, and $E[S_N] = N(2N+1)\lambda/6$. This entails that $E[\langle(\int \delta g_e)^2\rangle] = \langle g_e \rangle^2 N\lambda^2/12$.

The variance of $\langle(\int \delta g_e)^2\rangle$ is given by

$$\text{Var}\left[\left\langle\left(\int \delta g_e\right)^2\right\rangle\right] = \langle g_e \rangle^4 E\left[\left(\frac{N(N-1)\lambda^2}{12} + (N+1)\lambda\left(\frac{1}{N}\sum_{k=1}^N z_k\right) - \left(\frac{1}{N}\sum_{k=1}^N z_k\right)^2 + \frac{1}{N}\sum_{k=1}^N z_k^2 - 2\lambda S_N\right)^2\right]$$

Setting $\delta z_k = z_k - E[z_k]$, we rewrite the sum of the four first terms as $f(N) + \delta f(N)$ where

$$f(N) = \frac{N(2N+1)\lambda^2}{3} \quad (\text{A9})$$

$$\delta f(N) = \frac{(N+1)\lambda}{N} \sum_k \delta z_k + \frac{N-1}{N^2} \sum_k \left(\delta z_k^2 - \frac{N^2\lambda^2}{12}\right) - \frac{1}{N^2} \sum_{i,j,i \neq j} \delta z_i \delta z_j \quad (\text{A10})$$

Because $E[\delta f(N)] = 0$, we have

$$\text{Var}\left[\left\langle\left(\int \delta g_e\right)^2\right\rangle\right] = \langle g_e \rangle^4 \left(f(N)(f(N) - 4\lambda E[S_N]) + E[\delta f(N)^2] + 4\lambda^2 E[S_N^2] - 4\lambda E[\delta f(N)S_N]\right)$$

The first term is equal to $-f(N)^2$. Because the z_j are independent, centered and their probability density is an even function, the variance of $\delta f(N)$ is the sum of the variances of the three terms in equation (A10). It is equal to $(32N^3 + 61N^2 + 27N)\lambda^4/360$. The quantity $E[S_N^2]$ involves the second moments $E[y_j^2]$ and $E[y_j y_k]$ and can be expressed in terms of sums of positive powers $\sum_{k=1}^N k^p$ (Abramowitz and Stegun, 1970). One finds that $E[S_N^2] = (20N^4 + 24N^3 + 13N^2 + 3N)\lambda^2/180$. One computes similarly $E[\delta f(N)S_N]$, which involves all the moments of order 2 and 3 of the y_j . After lengthy calculations, one finds $(16N^3 + 31N^2 + 13N)\lambda^3/360$. Summing all these contributions, one finally obtains $\text{Var}\left[\left\langle\left(\int \delta g_e\right)^2\right\rangle\right] = \langle g_e \rangle^4 N(N-1)\lambda^4/360$.

Integrating equation (A6) yields

$$\iint \delta g_e(y) = \langle g_e \rangle \left[\lambda \sum_{k=1}^N (y - z_k) \Theta(y - z_k) + \frac{\lambda}{2} \sum_{k=1}^N z_k - \frac{N\lambda}{2} y - \frac{y^2}{2} + \frac{y}{N} \sum_{k=1}^N z_k - \frac{N^2\lambda^2}{12} - \frac{1}{2N} \sum_{k=1}^N z_k^2 \right]$$

which can be rewritten $\iint \delta g_e(y) = \langle g_e \rangle \sum_{k=1}^N \eta_k(y)$, where

$$\eta_k(y) = \lambda(y - z_k) \Theta(y - z_k) - \frac{y^2}{2N} + \frac{y}{N} \left(z_k - \frac{N\lambda}{2} \right) - \frac{1}{2N} \left(\delta z_k^2 - E[\delta z_k^2] \right)$$

are independent random functions. Because $E[(y - z_k) \Theta(y - z_k)] = y^2/2N\lambda$, these random functions are centered. Their variance is equal to $N^2\lambda^4/720$. It follows that $Var[\iint \delta g_e(y)] = N^3\lambda^4 \langle g_e \rangle^2 / 720$.

A.2 Active membrane properties

Homogenization can also be applied when synaptic activity provokes the voltage-dependent activation of NMDA receptors on an otherwise passive dendrite. We expand the potential as a power series in ϵ and perform the Taylor expansion of $h(V)$ in the nonlinear voltage evolution equation. Averaging the resulting equation, one shows that the first term of the expansion is governed by

$$\frac{1}{r_i} \frac{\partial^2 V_0}{\partial x^2} = c_m \frac{\partial V_0}{\partial t} + g_m V_0 + \langle g_e \rangle (V_0 - V_e) + \langle g_{NMDA} \rangle h(V_0) (V_0 - V_{NMDA}) + \langle g_i \rangle (V_0 - V_i) \quad (\text{A11})$$

The first order correction to V_0 satisfies

$$\frac{1}{r_i} \frac{\partial^2 V_1}{\partial x^2} = c_m \frac{\partial V_1}{\partial t} + \left(g_m + \langle g_e \rangle + \langle g_{NMDA} \rangle \left(h(V_0) + \frac{dh}{dV}(V_0) (V_0 - V_{NMDA}) \right) + \langle g_i \rangle \right) V_1 \quad (\text{A12})$$

When the voltage lies in a region of negative slope conductance, the solution $V_1 = 0$ is unstable and voltage rapidly evolves to a distant stable state. On the opposite, when the slope conductance is positive, $V_1 = 0$ is linearly stable, and the membrane adopts a stable state that differs from V_0 by the second order correction $\epsilon^2 V_2$. This correction is given by the equations

$$\begin{aligned} \frac{1}{r_i} \frac{\partial^2 \langle V_2 \rangle}{\partial x^2} &= c_m \frac{\partial \langle V_2 \rangle}{\partial t} + \left(g_m + \langle g_e \rangle + \langle g_{NMDA} \rangle \left(h(V_0) + \frac{dh}{dV}(V_0) (V_0 - V_{NMDA}) \right) + \langle g_i \rangle \right) \langle V_2 \rangle \\ &+ \langle \delta g_e \delta V_2 \rangle + \langle \delta g_{NMDA} \delta V_2 \rangle \left(h(V_0) + \frac{dh}{dV}(V_0) (V_0 - V_{NMDA}) \right) + \langle \delta g_i \delta V_2 \rangle \\ \delta V_2 &= r_i \iint \delta g_e (V_0 - V_e) + r_i \iint \delta g_{NMDA} h(V_0) (V_0 - V_{NMDA}) + r_i \iint \delta g_i (V_0 - V_i) \end{aligned}$$

from which we deduce equations (3.3) and (3.4).

Homogenization can also be used to compute how active dendritic conductances affects the voltage fluctuations elicited by the activation of discrete synapses. For simplicity, we restrict ourselves to AMPA synapses and to a single persistent current exhibiting no inactivation. We treat here a slightly more general case than presented in the Section 3 of the paper. Indeed, we assume that the activation kinetics of the voltage-dependent current is not instantaneous. Voltage is then governed by the cable equation

$$\frac{1}{r_i} \frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + g_m V + g_{nl}(x)z(V - V_{nl}) + g_e(x)(V - V_e) \quad (\text{A13})$$

supplemented with the kinetic equation

$$\tau_z(V) \frac{\partial z}{\partial t} = z_\infty(V) - z \quad (\text{A14})$$

for the activation variable of the inward current. Equation (A13) is nonlinear because of the voltage-dependent conductance. However, voltage fluctuations and corrections to the average potential for finite ϵ , are computed by linearizing the cable equation around the limiting solution V_0 .

Homogenization is performed as follows. One expands both the membrane voltage V and the gating variable z as power series in ϵ (i.e. $V = V_0 + \epsilon V_1 + \epsilon^2 V_2 + \dots$, $z = z_0 + \epsilon z_1 + \epsilon^2 z_2 + \dots$). Substituting into equations (A13-A14) leads to a hierarchy of equations for V and z . The first two equations of the hierarchy for V are the same as in the passive case. Accordingly, neither V_0 nor V_1 depend on the “fast” variable y . It follows that z_0 , which is governed by

$$\tau_z(V_0) \frac{\partial z_0}{\partial t} = z_\infty(V_0) - z_0 \quad (\text{A15})$$

does not depend on y either. Averaging then the third equation of the hierarchy for V

$$\frac{1}{r_i} \left(\frac{\partial^2 V_0}{\partial x^2} + \frac{\partial^2 V_2}{\partial y^2} \right) = c_m \frac{\partial V_0}{\partial t} + g_m V_0 + \langle g_{nl}(x, y) z_0 \rangle (V_0 - V_{nl}) + \langle g_e(x, y, t) \rangle (V_0 - V_e) \quad (\text{A16})$$

one obtains the cable equation

$$\frac{1}{r_i} \frac{\partial^2 V_0}{\partial x^2} = c_m \frac{\partial V_0}{\partial t} + g_m V_0 + \langle g_{nl} \rangle z_0 (V_0 - V_{nl}) + \langle g_e \rangle (V_0 - V_e) \quad (\text{A17})$$

The first corrections to the voltage and to the activation variable, ϵV_1 and ϵz_1 , satisfy the coupled linear equations

$$\begin{aligned}\frac{1}{r_i} \frac{\partial^2 V_1}{\partial x^2} &= c_m \frac{\partial V_1}{\partial t} + (g_m + \langle g_{nl} \rangle z_0 + \langle g_e \rangle) V_1 + \langle g_{nl} \rangle z_1 (V_0 - V_{nl}) \\ \tau_z(V_0) \frac{\partial z_1}{\partial t} &= -z_1 + \left(z'_\infty(V_0) - \frac{z_\infty(V_0) - z_0}{\tau_z(V_0)} \tau'_z(V_0) \right) V_1\end{aligned}$$

where z'_∞ and τ'_z designate the derivatives of z_∞ and τ_z . These equations do not incorporate source terms. This implies that $V_1 = z_1 = 0$ is a solution. It is linearly stable or unstable depending on whether the slope conductance is positive or negative. When it is unstable, first order perturbations grow exponentially with time and the expansions of V and z break down. This is because there is no stable state of the membrane near V_0 and the voltage rapidly drifts away to a distant stable state. On the opposite, when $V_1 = z_1 = 0$ is stable, the membrane settles in a stable state near (V_0, z_0) , and corrections to the voltage and to the gating variable z are of order ϵ^2 , as in the passive case.

These corrections are computed as follows. Subtracting (A17) from (A16) and integrating twice gives

$$\delta V_2(x, y, t) = r_i \iint \delta g_e(x, y, t) (V_0(x, t) - V_e) + r_i \iint \delta g_{nl}(x, y) z_0(x, t) (V_0(x, t) - V_{nl}) \quad (\text{A18})$$

When activation is instantaneous, $z_0(x, t) = z_\infty(V_0(x, t))$, and one obtains equation (3.8). Inserting equation (A18) into the evolution equation of V_2 , i.e. the fifth equation of the hierarchy for V , and averaging, one obtains the linear evolution equation

$$\frac{1}{r_i} \frac{\partial^2 \langle V_2 \rangle}{\partial x^2} = c_m \frac{\partial \langle V_2 \rangle}{\partial t} + (g_m + \langle g_{nl} \rangle z_0 + \langle g_e \rangle) \langle V_2 \rangle + \langle \delta g_e \delta V_2 \rangle + \langle \delta g_{nl} \delta V_2 \rangle z_0 + \langle g_{nl} z_2 \rangle (V_0 - V_{nl}) \quad (\text{A19})$$

where the second order corrections to the activation variable evolves according to

$$\tau_z(V_0) \frac{\partial z_2}{\partial t} = -z_2 + \left(z'_\infty(V_0) - \frac{z_\infty(V_0) - z_0}{\tau_z(V_0)} \tau'_z(V_0) \right) (\langle V_2 \rangle + \delta V_2) \quad (\text{A20})$$

When the activation kinetics is instantaneous, $z_2 = z'_\infty(V_0) (\langle V_2 \rangle + \delta V_2)$, and equation (3.7) is deduced from equations (A17) and (A19).

We now investigate how the velocity of propagating solutions is affected by small scale fluctuations of the synaptic conductance and of the active conductance. Because we take into account only one voltage-dependent current that is inward and does not inactivate, these solutions are not genuine spikes with finite width but traveling depolarization fronts. For simplicity, we assume now that the activation kinetics of the inward current is instantaneous, and we restrict ourselves to steady-state synaptic activity. In a frame moving at the constant velocity v , voltage evolution is then governed by the equation

$$\frac{1}{r_i} \frac{\partial^2 V}{\partial \xi^2} + c_m v \frac{\partial V}{\partial \xi} = c_m \frac{\partial V}{\partial t} + g_m V + g_{nl}(\xi + vt)U(V) + g_e(\xi + vt)(V - V_e) \quad (\text{A21})$$

where $\xi = x - vt$ and $U(V) = z_\infty(V)(V - V_{nl})$. We apply the homogenization method to this equation. We introduce the fast coordinate $\eta = \xi/\epsilon$, replace the spatial derivatives $\partial/\partial \xi$ and $\partial^2/\partial \xi^2$ by $\partial/\partial \xi + (1/\epsilon)\partial/\partial \eta$ and $\partial^2/\partial \xi^2 + (2/\epsilon)\partial^2/\partial \xi \partial \eta + (1/\epsilon^2)\partial^2/\partial \eta^2$, and we expand the membrane voltage as a power series in the small parameter ϵ . Because conductance fluctuations may affect the front velocity, we also expand v as a power series in ϵ : $v = v_0 + \epsilon v_1 + \epsilon^2 v_2 + \dots$. In the $\epsilon = 0$ limit, the membrane voltage V_0 is governed by the equation

$$\frac{1}{r_i} \frac{\partial^2 V_0}{\partial \xi^2} + c_m v_0 \frac{\partial V_0}{\partial \xi} = c_m \frac{\partial V_0}{\partial t} + g_m V_0 + \langle g_{nl} \rangle U(V_0) + \langle g_e \rangle (V_0 - V_e) \quad (\text{A22})$$

The average conductances do not depend on time. Indeed, a change in time amounts to a shift in space and does not affect $\langle g_{nl} \rangle$ and $\langle g_e \rangle$, which are stationary in space. If v is the front velocity, the voltage profile becomes stationary in the moving frame, and it is given by the *ordinary* differential equation

$$\frac{1}{r_i} \frac{d^2 V_0}{d\xi^2} + c_m v_0 \frac{dV_0}{d\xi} - g_m V_0 - \langle g_{nl} \rangle U(V_0) - \langle g_e \rangle (V_0 - V_e) = 0 \quad (\text{A23})$$

The propagating front is a linearly stable solution of equation (A21). This is proved as in van Saarloos (1998). We add to $V_0(\xi)$ a small perturbation $\zeta(\xi)e^{-Et/\tau_m}$, where $\tau_m = c_m/g_m$ is the membrane time constant, and we linearize equation (A21) around V_0 . We obtain the eigenvalue equation $\mathcal{L}[\zeta] = -E\zeta$ where

$$\mathcal{L}[\zeta] = \frac{1}{r_i g_m} \frac{\partial^2 \zeta}{\partial \xi^2} + v_0 \tau_m \frac{\partial \zeta}{\partial \xi} - \left(g_m + \langle g_e \rangle + \langle g_{nl} \rangle \frac{dU(V_0)}{dV} \right) \frac{\zeta}{g_m}$$

The drift term $v_0\tau_m\partial\zeta/\partial\xi$ is eliminated by setting $\zeta(\xi, t) = e^{-\tau_mv_0\xi/2\lambda^2}\Psi(\xi)$. The eigenvalue equation then becomes $\mathcal{H}\Psi = E\Psi$ where

$$\mathcal{H}\Psi = -\lambda^2\frac{d^2\Psi}{d\xi^2} + \left(1 + \frac{\langle g_e \rangle}{g_m} - \left(\frac{\tau_mv}{2\lambda}\right)^2 + \frac{\langle g_{nl} \rangle}{g_m} \frac{dU(V_0)}{dV}\right)\Psi$$

Formally, this is the same Schrödinger eigenvalue problem as when determining the energy levels, E , of a quantum particle moving in a potential well U (Landau and Lifshitz, 1977). Because equation (A21) is translation invariant, it is satisfied not only by $V_0(\xi)$ but also by any shifted function $V_0(\xi+a)$. This marginal stability implies that one of the eigenvalues of \mathcal{L} , E_0 , is null with associated eigenfunction $dV_0(\xi)/d\xi$. The corresponding eigenfunction of \mathcal{H} is then $\Psi_0(\xi) = e^{\tau_mv_0\xi/2\lambda^2}dV_0(\xi)/d\xi$. Because V_0 is a monotonic function of ξ , $\Psi_0(\xi)$ does not vanish. This implies that $E_0 = 0$ is the ground state of the Schrödinger eigenvalue problem, that all other energy levels, E_n ($n \geq 1$), are positive, and that the gap between E_0 and the first excited level E_1 is finite (Landau and Lifshitz, 1977). Therefore, the front is linearly stable with respect to all the perturbations that do not amount to mere shift of the voltage profile.

Next, we compute the corrections to the front voltage profile for finite ϵ . At order ϵ , the voltage does not display small scale fluctuations, and the front profile $V(\xi) = V_0(\xi) + \epsilon V_1(\xi)$ satisfies

$$\frac{1}{r_i} \frac{d^2V}{d\xi^2} + c_m(v_0 + \epsilon v_1) \frac{dV}{d\xi} - g_m V - \langle g_{nl} \rangle U(V) - \langle g_e \rangle (V - V_e) = 0$$

In this equation, ϵv_1 is the correction to the velocity that is required to make the front stationary in the moving frame. Subtracting equation (A23) one obtains the equation $\mathcal{L}[V_1] = -v_1\tau_m dV_0/d\xi$ for the voltage correction. It follows that V_1 is proportional to the null eigenvector $dV_0/d\xi$ and that $v_1 = 0$. Thus, it corresponds to a mere shift of amplitude ϵ of the front $V_0(\xi)$ and does not constitute a genuine correction to the voltage profile. Relevant voltage corrections appear only at order ϵ^2 .

At this order, the propagating front exhibits small scale fluctuations, which are given by

$$\delta V_2 = r_i \iint \delta g_{nl} U(V_0) + r_i \iint \delta g_e (V_0 - V_e)$$

In addition, the profile of the moving front and its velocity are slightly altered. The correction $\langle V_2 \rangle$ satisfies

$$\begin{aligned} \mathcal{L} \langle V_2 \rangle = -v_2 \tau_m \frac{dV_0}{d\xi} & - \frac{\left\langle \left(\int \delta g_{nl} \right)^2 \right\rangle}{2g_m^2 \lambda^2} \frac{dU^2(V_0)}{dV} - \frac{\left\langle \left(\int \delta g_e \right)^2 \right\rangle}{g_m^2 \lambda^2} (V_0 - V_e) \\ & - \frac{\left\langle \int \delta g_{nl} \int \delta g_e \right\rangle}{g_m^2 \lambda^2} \frac{d(U(V_0)(V_0 - V_e))}{dV} \end{aligned} \quad (\text{A24})$$

where the velocity correction $\epsilon^2 v_2$ is such that it makes the average voltage profile $V_0 + \epsilon^2 \langle V_2 \rangle$ stationary in the moving frame. To determine this correction, one projects equation (A24) onto the null eigenvector $dV_0/d\xi$ of \mathcal{L} . This gives

$$\begin{aligned} v_2 = \frac{r_i}{2c_m \int_{-\infty}^{\infty} (dV_0/d\xi)^2 d\xi} \cdot & \left(\left\langle \left(\int \delta g_{nl} \right)^2 \right\rangle (U^2(V_{peak}) - U^2(V_{rest})) \right. \\ & + \left\langle \left(\int \delta g_e \right)^2 \right\rangle ((V_{peak} - V_e)^2 - (V_{rest} - V_e)^2) \\ & \left. + 2 \left\langle \int \delta g_{nl} \int \delta g_e \right\rangle (U(V_{peak})(V_{peak} - V_e) - U(V_{rest})(V_{rest} - V_e)) \right) \end{aligned} \quad (\text{A25})$$

where $V_{rest} = V_0(\infty)$ and $V_{peak} = V_0(-\infty)$ are solutions of the equation

$$g_m V + \langle g_{nl} \rangle U(V) = \langle g_e \rangle (V_e - V) \quad (\text{A26})$$

which is deduced from (A23). The modification $\epsilon^2 \langle V_2 \rangle$ of the front profile is then computed by solving equation (A24). Only the projection of $\langle V_2 \rangle$ onto the eigenvectors of \mathcal{L} associated with non-zero eigenvalues is relevant, the projection onto the null eigenvector corresponding to a shift in space of the front. The average voltage profile, $V_0 + \epsilon^2 \langle V_2 \rangle$, is still stable for finite ϵ . Indeed, the linear stability of the front is determined by the operator \mathcal{L} , as in the $\epsilon = 0$ limit.

The velocity correction is the sum of three terms, corresponding to the spatial fluctuations of the active conductance, to the fluctuations of the synaptic conductance, and to the spatial correlations between these two conductances. In the absence of synaptic activity, only the first term remains. Equation (A26) reduces

to $\langle g_{nl} \rangle U(V) = -g_m V$, and we have

$$v_2 = \frac{1}{2\lambda^2\tau_m \int_{-\infty}^{\infty} (dV_0/d\xi)^2 d\xi} \frac{\langle (\int \delta g_{nl})^2 \rangle}{\langle g_{nl} \rangle^2} (V_{peak}^2 - V_{rest}^2)$$

Because the propagating front depolarizes the membrane, V_{rest} is smaller than V_{peak} and v_2 is positive. This shows that heterogeneities of the nonlinear conductance, by themselves, increase the front velocity. In contrast, when the nonlinear conductance is uniformly distributed along the dendrite, the front velocity is only perturbed by the spatial variations of the excitatory synaptic activity. The velocity correction is given by the second term in equation (A25) and is equal to

$$v_2 = \frac{r_i}{2c_m \int_{-\infty}^{\infty} (dV_0/d\xi)^2 d\xi} \left\langle \left(\int \delta g_e \right)^2 \right\rangle (V_{peak} - V_{rest}) \left((V_{peak} - V_{rest}) - 2(V_e - V_{rest}) \right)$$

Conductance fluctuations increase the front velocity if the front amplitude $V_{peak} - V_{rest}$ is at least twice as large as the synaptic driving force $V_e - V_{rest}$ and decrease it in the opposite case. When both the nonlinear conductance and the synaptic conductance fluctuate at small scale, all three terms must be taken into account in equation (A25). Using equation (A26), one shows that, when synaptic activity is intense, the last term behaves as $-\left(r_i/c_m \int_{-\infty}^{\infty} (dV_0/d\xi)^2 d\xi\right) \left(\langle \int \delta g_{nl} \int \delta g_e \rangle \langle g_e \rangle / \langle g_{nl} \rangle \right) (V_{peak} - V_{rest}) \left((V_{peak} - V_{rest}) - 2(V_e - V_{rest}) \right)$. This term tends to compensate the second term when the fluctuations of the active and synaptic conductances are positively correlated, while the two terms add their effects when the fluctuations are negatively correlated. Finally, we remark that inhibitory synapses will have a greater impact than the excitatory synapses considered above, because their driving force is negative. The largest velocity increase will be obtained when synaptic inhibition is strong and anti-correlated with the spatial fluctuations of the depolarizing voltage-dependent conductance responsible.

A.3 Spiny dendrites

This appendix shows how to apply homogenization to a dendrite densely covered with spines. To make equations more compact, we introduce the linear operator $\mathcal{L}[V] = \tau_m \partial V / \partial t + V$, which governs passive

voltage relaxation. Equations (4.1) and (4.2) are rewritten as

$$\frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} = g_m \mathcal{L}[V_d] + g_i (V_d - V_i) + \rho G_c (V_d - V_s) \quad (\text{A27})$$

$$0 = (G_c + G_e + G_s \mathcal{L}) [V_s] - G_c V_d - G_e V_e \quad (\text{A28})$$

From equation (A28), we have

$$V_s = (G_c + G_e + G_s \mathcal{L})^{-1} [G_c V_d + G_e V_e] \quad (\text{A29})$$

for the spine voltage and

$$V_s - V_d = \left(G_c (G_c + G_e + G_s \mathcal{L})^{-1} [V_d] - V_d \right) + (G_c + G_e + G_s \mathcal{L})^{-1} [G_e] V_e \quad (\text{A30})$$

for the voltage drop between spine and dendrite. Substituting this last expression into (A27), we obtain the closed equation

$$\begin{aligned} \frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} &= g_m \mathcal{L}[V_d] + g_i (V_d - V_i) + \rho G_c \left(1 - G_c (G_c + G_e + G_s \mathcal{L})^{-1} \right) [V_d] \\ &- \rho G_c (G_c + G_e + G_s \mathcal{L})^{-1} [G_e] V_e \end{aligned} \quad (\text{A31})$$

for the dendritic voltage.

The current $I_c = \rho G_c (V_s - V_d)$ flowing from the spines to the dendrite (per unit length) reads

$$I_c = -\rho G_c \left(V_d - (G_c + G_e + G_s \mathcal{L})^{-1} [G_e] V_e \right) + \rho G_c^2 (G_c + G_e + G_s \mathcal{L})^{-1} [V_d] \quad (\text{A32})$$

This coupling current goes to infinity with the average spine density $\langle \rho \rangle$ as ϵ goes to 0 if all other parameters are kept constant. If G_c is kept fixed, G_e must scale as ϵ to compensate the divergence of the coupling current. The spine voltage is then governed by the strong coupling with the dendritic shaft ($G_c \gg G_s + G_e$). Expanding the operator $G_c (G_c + G_e + G_s \mathcal{L})^{-1}$ as $1 - (G_e + G_s \mathcal{L}) / G_c + (G_e + G_s \mathcal{L})^2 / G_c^2 + \dots$, one finds that $V_s \approx V_d - G_s \mathcal{L}[V_d] / G_c + G_e (V_e - V_d) / G_c$. When ϵ goes to 0, the spine head voltage tends to V_d and I_c behaves as $-\rho G_s \mathcal{L} V_d + \rho G_e (V_e - V_d)$.

Homogenization is performed very much as in the case of conductance fluctuations. One sets $y = x/\epsilon$, expands the voltage as $V_d = V_0 + \epsilon V_1 + \epsilon^2 V_2 + \dots$, and one derives from (A27) a hierarchy of voltage equations, keeping in mind that ρ , G_e , C_s and G_s all depend on ϵ and that G_e may depend on time. The first two equations of the hierarchy read $\partial^2 V_0/\partial y^2 = 0$ and $\partial^2 V_1/\partial y^2 + 2\partial^2 V_0/\partial x\partial y = 0$, which implies that V_0 and V_1 , are both independent of y and that voltage fluctuations appear only at order ϵ^2 . The evolution equation of the leading term $V_0(x, t)$ is obtained by averaging the third equation of the hierarchy (i.e. the equation of evolution at order 1)

$$\frac{1}{r_i} \left(\frac{\partial^2 V_0}{\partial x^2} + \frac{\partial V_2}{\partial y^2} \right) = (g_m + \rho G_s) \mathcal{L}V_0 + \rho G_e (V_0 - V_e) + g_i (V_0 - V_i) \quad (\text{A33})$$

which gives

$$\frac{1}{r_i} \frac{\partial^2 V_0}{\partial x^2} = (g_m + \langle \rho G_s \rangle) \mathcal{L}V_0 + \langle \rho G_e \rangle (V_0 - V_e) + \langle g_i \rangle (V_0 - V_i) \quad (\text{A34})$$

Replacing \mathcal{L} by $(C_m/G_m)\partial/\partial t + 1$, one obtains the equation (4.3). Subtracting this equation from equation (A33) and integrating twice, one obtains equation (4.4). Finally, expanding the voltage evolution equation at order ϵ and averaging, one obtains

$$\begin{aligned} \frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} &= \left(g_m + \langle \rho G_s \rangle - 2 \left\langle \frac{\rho G_s G_e}{G_c} \right\rangle \right) \mathcal{L}V_d + \left\langle \frac{\rho G_s G_e}{G_c} \right\rangle V_d - \left\langle \frac{\rho G_s^2}{G_c} \right\rangle \mathcal{L}^2 V_d + \langle g_i \rangle (V_d - V_i) \\ &+ \left(\langle \rho G_e \rangle - \left\langle \frac{\rho G_e^2}{G_c} \right\rangle - \left\langle \frac{\rho G_s}{G_c} \mathcal{L}[G_e] \right\rangle \right) (V_d - V_e) \end{aligned}$$

where $V_d = V_0 + \epsilon V_1$. This gives the equation (4.5).

To avoid the divergence of the coupling current, one may also assume that G_c scales as ϵ , which entails that the coupling conductance per unit length $\langle \rho G_c \rangle$ remains bounded. Because the spines are weakly coupled to the dendritic shaft, their voltage is essentially determined by the excitatory synaptic input they receive. Expanding the operator $(G_c + G_e + G_s \mathcal{L})^{-1}$ in equation (A28) in powers of ϵ , we have

$$V_s \approx V_e - \frac{G_c + G_s}{G_e} V_e \quad (\text{A35})$$

The influence of the dendritic voltage appears only at order ϵ^2 . When ϵ goes to 0, G_c and G_s both go to

0, and the spine voltage tends to the synaptic reversal potential V_e . Spines are thus decoupled from the dendritic shaft. In contrast, the dendritic shaft still feels the summed effects of the spines. The weakness of the current $G_c(V_s - V_d)$ flowing from any single spine to the shaft is compensated by the high density of spines; and the coupling current per unit length, $I_c = \langle \rho G_c (V_s - V_d) \rangle$ does not vanish.

Homogenization is performed as in the strong coupling regime, but the hierarchy of equations obtained is not the same, because of the different scaling with ϵ of G_c , and G_e . Averaging the third equation

$$\frac{1}{r_i} \left(\frac{\partial^2 V_0}{\partial x^2} + 2 \frac{\partial^2 V_1}{\partial x \partial y} + \frac{\partial^2 V_2}{\partial y^2} \right) = g_m \mathcal{L}[V_0] + \rho G_c (V_0 - V_s) + g_i (V_0 - V_i) \quad (\text{A36})$$

gives

$$\frac{1}{r_i} \frac{\partial^2 V_0}{\partial x^2} = g_m \mathcal{L}[V_0] + \langle \rho G_c \rangle (V_0 - V_s) + \langle g_i \rangle (V_0 - V_i) \quad (\text{A37})$$

Replacing $\mathcal{L}[V]$ by $(C_m/G_m) \partial V / \partial t + V$ and V_s by V_e , one obtains equation (4.6). When the voltage correction ϵV_1 , is taken into account, the average voltage $\langle V_d \rangle = V_0 + \epsilon V_1$ still satisfies equation (A37), but one must now incorporate the first order corrections to V_s given by equation (A35). Equation (4.8) follows. Finally, subtracting (A37) from (A36) and integrating twice, one obtains equation (4.7) for the small scale voltage fluctuations.

When all three conductances G_c , G_s and G_e scale as ϵ , the coupling current also remains finite. the voltage drop between spines and dendrite remains finite, and I_c is given by the full equation (A32). Homogenization leads to the voltage evolution equation

$$\begin{aligned} \frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} &= g_m \mathcal{L}[V_d] + \langle \rho G_c \rangle V_d - \left\langle \rho G_c^2 (G_c + G_e + G_s \mathcal{L})^{-1} [V_d] \right\rangle + \langle g_i \rangle (V_d - V_i) \\ &- \left\langle \rho G_c (G_c + G_e + G_s \mathcal{L})^{-1} [G_e] V_e \right\rangle \end{aligned} \quad (\text{A38})$$

in the $\epsilon = 0$ limit. It involves the filtering term

$$(G_c + G_e + G_s \mathcal{L})^{-1} [V_d] = \int_{-\infty}^t V_d(t') e^{-\int_r^t (G_c + G_s + G_e(t'')) dt'' / C_s} dt' / C_s$$

and is therefore an integro-differential equation. Alternatively, equation (A38) can be rewritten as the

coupled system

$$\begin{aligned}\frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} &= c_m \frac{\partial V_d}{\partial t} + g_m V_d + \langle g_i \rangle (V_d - V_i) + \langle \rho G_c \rangle (V_d - V_s) \\ 0 &= \langle C_s \rangle \frac{\partial V_s}{\partial t} + \langle G_s \rangle V_s + \langle G_c \rangle (V_s - V_d) + \langle G_e \rangle (V_s - V_e)\end{aligned}$$

which describes a continuum of spines, with head conductance $\langle G_s \rangle + \langle G_e \rangle$, coupled to the dendritic shaft via the average conductance $\langle \rho G_c \rangle$. Only in steady-state conditions, does one obtain a standard diffusion equation

$$\frac{1}{r_i} \frac{\partial^2 V_d}{\partial x^2} = g_m V_d + \langle \rho G_c \rangle V_d - \left\langle \frac{\rho G_c^2}{G_c + G_e + G_s} \right\rangle V_d - \left\langle \frac{\rho G_c G_e}{G_c + G_e + G_s} G_e \right\rangle V_e + \langle g_i \rangle (V_d - V_i)$$

for the voltage of the dendrite.

A.4 Varicose dendrites

In this appendix, we apply homogenization to a passive dendrite displaying a string of synaptic varicosities. Homogenization is performed as in Appendix A.1 and leads to a hierarchy of voltage equations. The first three of them read

$$\frac{\partial}{\partial y} \left(\frac{1}{r_i(x, y)} \frac{\partial V_0}{\partial y} \right) = 0 \quad (\text{A39})$$

$$\frac{\partial}{\partial y} \left(\frac{1}{r_i(x, y)} \left(\frac{\partial V_0}{\partial x} + \frac{\partial V_1}{\partial y} \right) \right) + \frac{\partial}{\partial x} \left(\frac{1}{r_i(x, y)} \frac{\partial V_0}{\partial y} \right) = 0 \quad (\text{A40})$$

$$\frac{\partial}{\partial x} \left(\frac{1}{r_i(x, y)} \left(\frac{\partial V_0}{\partial x} + \frac{\partial V_1}{\partial y} \right) \right) + \frac{\partial}{\partial y} \left(\frac{1}{r_i(x, y)} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) \right) = C_m \frac{\partial V_0}{\partial t} + G_m V_0 + G_e (V_0 - V_e) \quad (\text{A41})$$

Higher order equations are similar to equation (A41): V_0 , V_1 and V_2 are just replaced by V_n , V_{n+1} and V_{n+2} ($n \geq 1$) and the term $G_e V_e$ is omitted.

Integrating equation (A39) yields $\partial V_0(x, y, t)/\partial y = f_0(x, t)r_i(x, y)$, where $f_0(x, t)$ is some unknown function. Because the average $\partial V_0/\partial y$ is zero and the axial resistance is positive, f_0 is necessarily zero and thus V_0 does not depend on y . Integrating (A40), we obtain $\partial V_1(x, y, t)/\partial y = f_1(x, t)r_i(x, y) - \partial V_0(x, t)/\partial x$.

Averaging over y gives $f_1 = (\partial V_0 / \partial x) / \langle r_i \rangle$, from which we deduce

$$\frac{\partial V_1}{\partial y} = \left(\frac{r_i}{\langle r_i \rangle} - 1 \right) \frac{\partial V_0}{\partial x} \quad (\text{A42})$$

and, by integrating over y , the equation (5.5). Finally, substituting equation (A42) in equation (A41) and averaging, one obtains the equation (5.3), which reduces to equation (5.2) when the diameter is uniform in average.

The time evolution of V_1 is governed by the fourth equation of the hierarchy

$$\frac{\partial}{\partial x} \left(\frac{1}{r_i} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) \right) + \frac{\partial}{\partial y} \left(\frac{1}{r_i} \left(\frac{\partial V_2}{\partial x} + \frac{\partial V_3}{\partial y} \right) \right) = C_m \frac{\partial V_1}{\partial t} + G_m V_1 + G_e V_1 \quad (\text{A43})$$

Averaging over y yields

$$\frac{\partial}{\partial x} \left(\left\langle \frac{1}{r_i} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) \right\rangle \right) = \langle C_m \rangle \frac{\partial \langle V_1 \rangle}{\partial t} + \langle G_m \rangle \langle V_1 \rangle + \langle G_e \rangle \langle V_1 \rangle + \left\langle C_m \frac{\partial \delta V_1}{\partial t} + G_m \delta V_1 + G_e \delta V_1 \right\rangle \quad (\text{A44})$$

Using equations (5.3) and (5.5), we deduce from equation (A41) that

$$\frac{\partial}{\partial y} \left(\frac{1}{r_i} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) \right) = \delta C_m \frac{\partial V_0}{\partial t} + \delta G_m V_0 + \delta G_e (V_0 - V_e)$$

Exploiting the relations $\delta C_m = C_m \delta S / \langle S \rangle$ and $\delta G_m = G_m \delta S / \langle S \rangle$, which stem from the uniformity of the specific capacitance and conductance, and using once again equation (5.3), the equation above becomes

$$\frac{\partial}{\partial y} \left(\frac{1}{r_i} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) \right) = \frac{\delta S}{\langle S \rangle} \frac{\partial}{\partial x} \left(\frac{1}{\langle r_i \rangle} \frac{\partial V_0}{\partial x} \right) + \left(\delta G_e - \frac{\langle G_e \rangle}{\langle S \rangle} \delta S \right) (V_0 - V_e)$$

Integrating it, one obtains

$$\frac{1}{r_i} \left(\frac{\partial V_1}{\partial x} + \frac{\partial V_2}{\partial y} \right) = \frac{\int \delta S}{\langle S \rangle} \frac{\partial}{\partial x} \left(\frac{1}{\langle r_i \rangle} \frac{\partial V_0}{\partial x} \right) + \left(\int \delta G_e - \frac{\langle G_e \rangle}{\langle S \rangle} \int \delta S \right) (V_0 - V_e) + f_2(x, t)$$

where

$$f_2(x, t) = \frac{1}{\langle r_i \rangle} \frac{\partial \langle V_1 \rangle}{\partial x} - \frac{1}{\langle r_i \rangle \langle S \rangle} \left(\left\langle r_i \int \delta S \right\rangle \frac{\partial}{\partial x} \left(\frac{1}{\langle r_i \rangle} \frac{\partial V_0}{\partial x} \right) + \left\langle r_i \int (\delta G_e \langle S \rangle - \langle G_e \rangle \delta S) \right\rangle (V_0 - V_e) \right)$$

Replacing the left hand side of equation (A44) by $\partial f_2 / \partial x$ and using one more time equations (5.3) and (5.5), one obtains

$$\begin{aligned} \frac{\partial}{\partial x} \left(\frac{1}{\langle r_i \rangle} \frac{\partial \langle V_1 \rangle}{\partial x} \right) &= \langle C_m \rangle \frac{\partial \langle V_1 \rangle}{\partial t} + \langle G_m \rangle \langle V_1 \rangle + \langle G_e \rangle \langle V_1 \rangle - \frac{1}{\langle S \rangle} \frac{\partial}{\partial x} \left(\frac{\langle \delta S \int \delta r_i \rangle}{\langle r_i \rangle} \right) \frac{\partial}{\partial x} \left(\frac{1}{\langle r_i \rangle} \frac{\partial V_0}{\partial x} \right) \\ &\quad - \left(\frac{\langle \delta S \int \delta r_i \rangle}{\langle r_i \rangle \langle S \rangle} \left(\frac{\partial \langle G_e \rangle}{\partial x} - \frac{\langle G_e \rangle}{\langle S \rangle} \frac{\partial \langle S \rangle}{\partial x} \right) + \frac{\partial}{\partial x} \frac{\langle (\delta G_e - \langle G_e \rangle \delta S / \langle S \rangle) \int \delta r_i \rangle}{\langle r_i \rangle} \right) (V_0 - V_e) \end{aligned}$$

Multiplying it by ϵ and adding to (5.1), one finally gets equation (5.4).

We now estimate the size of the small scale voltage fluctuations for different spatial distributions of the varicosities. The relative amplitude of voltage fluctuations, compared to the average potential, is controlled by the quantity $\epsilon \int \delta r_i / \langle r_i \rangle$. The integral has the same expression as the integral $\int \delta G_e / \langle G_e \rangle$ in Section 2. Therefore, we may partly capitalize on the results of this section. We consider first point varicosities described by Dirac functions and then discuss how the results thus obtained are modified by varicosities of finite width.

For a periodic distribution of point varicosities, the integral is also periodic and equal to $\lambda/2 - y$ on $[0, \lambda]$. This entails that voltage fluctuations scale as L/N . When the periodic distribution is perturbed by a random jitter ξ_k , $1 \leq k \leq N$, the integral is modified by the additional terms $\lambda \sum_{k=1}^N \chi_k(y) + \lambda \sum_{k=1}^N \xi_k / N$, where, as in Appendix A.1, χ_k is the difference of two Heaviside functions and is non-zero only near the k -th varicosity. It follows that between varicosities, the expectation of $\int \delta r_i / \langle r_i \rangle$ is equal to $\lambda/2 - y$ and its variance behaves as $\lambda^2 \text{Var}[\xi_k] / N$ for large N . As expected, one recovers the results obtained for the periodic distribution. Near the k -th varicosity, the expectation of $\int \delta r_i / \langle r_i \rangle$ is equal $\lambda/2 - y + E[\chi_k(y)]$, and its variance behaves as $\lambda^2 \text{Var}[\chi_k]$ for large N . Both moments remains finite. It follows that voltage fluctuations still scale as L/N as in the periodic case.

In contrast, voltage fluctuations display a different scaling for a random distribution of point varicosities with uniform density. The integral is then equal to $(\lambda \sum_{k=1}^N \theta(y - z_k) - y) - (N\lambda/2 - \sum_{k=1}^N z_k)$, where the independent random variables z_k denote the locations of varicosities in their drawing order. As $E[z_k] = N\lambda/2$ and $E[\theta(y - z_k)] = y/N\lambda$, the expectation of the integral is zero. Using then the formulae $E[z_k^2] = N^2\lambda^2/3$ and $E[z_k\theta(y - z_k)] = y^2/2N\lambda$, one shows that the variance of the integral is equal to $N^2\lambda^2/12$, independently of y . It follows that the relative amplitude of the voltage fluctuations, as estimated by the standard deviation of $\epsilon \int \delta r_i / \langle r_i \rangle$, scales as L / \sqrt{N} .

When the width of varicosities is taken into account, the filling factor f becomes positive. Let r be the ratio of the diameter d_+ of varicosities to the diameter d_- of constrictions. The average diameter is then $\langle d \rangle = d_+f + d_-(1-f)$, and the axial resistance r_i varies between $4R_i/\pi d_+^2 = 4R_i(1-f+rf)^2/\pi r^2 \langle d \rangle^2$ (for varicosities) and $4R_i/\pi d_-^2 = 4R_i(1-f+rf)^2/\pi \langle d \rangle^2$ (for constrictions), where R_i is the cytoplasmic resistivity. The amplitude of fluctuations is thus equal to $4R_i(r^2-1)(1-f+rf)^2/\pi r^2 \langle d \rangle^2$ and depends on the average diameter of the dendrite. In contrast, the average axial resistance $\langle r_i \rangle = 4R_i \langle 1/\pi d^2 \rangle$ depends on the harmonic mean $\langle \pi d^2 \rangle_h = 1/\langle 1/\pi d^2 \rangle$ of the cross-section, which is equal to $\pi r^2 \langle d \rangle^2 / ((f + (1-f)r^2)(1-f+rf)^2)$. It follows that the relative amplitude of axial resistance is equal to $(r^2-1)/(f+(1-f)r^2)$. It is independent of the average diameter and increases with both r and f .

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