Time Fractional Cable Equation And Applications in Neurophysiology

Silvia Vitali\textsuperscript{a,}\textsuperscript{*}, Gastone Castellani\textsuperscript{a}, Francesco Mainardi\textsuperscript{b}

\textsuperscript{a} Viale Berti Pichat 6/2, Bologna, DIFA
\textsuperscript{b} via Irnerio 46, Bologna, DIFA

Abstract

We propose an extension of the cable equation by introducing a Caputo time fractional derivative. The fundamental solutions of the most common boundary problems are derived analytically via Laplace Transform, and result be written in terms of known special functions. This generalization could be useful to describe anomalous diffusion phenomena with leakage as signal conduction in spiny dendrites. The presented solutions are computed in Matlab and plotted.

Keywords: Fractional cable equation, Sub-diffusion, Wright functions, Laplace transform, Efros Theorem, Dendrites

1. Introduction

The one dimensional cable model is treated in standard textbooks of neurophysiology to model the electrical conduction of non-isopotential excitable cells. In particular it describes the spatial and the temporal dependence of transmembrane potential $V_m(x,t)$ along the axial $x$ direction of a cylindrical nerve cell segment. The membrane behaviour is summarized by an electrical circuit with an axial internal resistance $r_i$, and a transmembrane capacitance $c_m$ and a transmembrane resistance $r_m$ in parallel, connecting the inner part to the outside. External axial resistance could be eventually included. Transmembrane

\textsuperscript{*}Corresponding author

Email address: silvia.vitali4@unibo.it (Silvia Vitali)
URL: www.fracalmo.org (Francesco Mainardi)
potential is generated by ionic concentration gradient across the membrane, and is maintained non null at rest (no current) by a combination of passive and active cell mechanisms. Equivalent models can in fact be derived from the Nernst-Planck equation for electro-diffusive motion of ions.

Cell excitation can be caused by electro stimulation of the membrane. The consequent variation in transmembrane potential is transmitted along the cell segment. The resulting differential equation for the trans-membrane potential takes the form of a standard diffusion equation with an extra a term to account leakage of ions out of the membrane, it results in a decay of the electric signal in space and in time:

$$\lambda^2 \frac{\partial^2 V_m(x, t)}{\partial x^2} - \kappa \frac{\partial V_m(x, t)}{\partial t} - V_m(x, t) = 0,$$

$$\lambda = \sqrt{r_m/r_i}$$ and $$\kappa = r_m c_m$$ are space and time constants related to the membrane resistance and capacitance per unit length, see e.g. [12]. For simplicity in the rest of this work, following [12], we will use the dimensionless scaled variables $$X = x/\lambda$$ and $$T = t/\kappa$$, so that we consider the equation

$$\frac{\partial^2 V_m(X, T)}{\partial X^2} - \frac{\partial V_m(X, T)}{\partial T} - V_m(X, T) = 0.$$  

Some interesting quantities to neurophysiology are connected to First kind boundary condition (the Signal Problem) and Second Kind boundary condition problems. Signal Problem is interesting to understand how the system evolves when excited at one end with a specific potential profile, Second Kind boundary condition problem is interesting because can be related to the profile of a current injected across the membrane.

In signalling problems the cable is considered of semi-infinite length ($0 \leq X < \infty$), initially quiescent for $$T < 0$$ and excited for $$T \geq 0$$ at the accessible end ($X = 0$) with a given input in membrane potential $$V_m(0, T) = g(t)$$. The solution can be derived via the Laplace Transform (LT) approach:

$$\frac{\partial^2 V_m(X, T)}{\partial X^2} = (s + 1)V_m(X, T),$$

and the LT of the solution results

$$\tilde{V}_m(X, s) = g(s)e^{-\sqrt{s+1}X}.$$
Relevant cases are impulsive input $g(t) = \delta(t)$ and unit step input $g(t) = \theta(t)$ where $\delta(t)$ and $\theta(t)$ denote the Dirac and the Heaviside functions, respectively. The solutions corresponding to these inputs can be obtained by LT inversion \[12\] and read in our notation

$$G_s(X,T) = \frac{X}{\sqrt{4\pi T^3}} e^{-(X^2/4T+T)}, \quad (5)$$

and

$$H_s(X,T) = \int_0^T G_s(X,T') dT'. \quad (6)$$

We refer to $G_s$ to as the fundamental solution or the Green function for the signalling problem of the (linear) cable equation (Eq.2), whereas to $H_s$ to as the step response. As known, the Green function is used in the time convolution integral to represent the solution corresponding to any given input $g(T)$ as follows

$$V_m(X,T) = \int_0^T g(T-T') G_s(X,T') dT'. \quad (7)$$

The spatial variance associated to this model is known to evolve linearly in time.

If we consider an impulse or a step current injected at some point $X$ the problem is subjected to the following boundary conditions, specifically

$$I = I_0 \delta(T) = \frac{-1}{r_i \lambda} \frac{\partial V_m(X,T)}{\partial X}, \quad (8)$$

or

$$I = I_0 \theta(T) = \frac{-1}{r_i \lambda} \frac{\partial V_m(X,T)}{\partial X}. \quad (9)$$

We consider the adimensional current $I = I_0 r_i \lambda$ and put it to unity for convenience. Applying the impulse in $X = 0$ the LT reduces to

$$\tilde{V}_m(X,s) = \frac{1}{\sqrt{s+1}} e^{-\sqrt{s+1}X}, \quad (10)$$

the Green function and the step response function (when a step current is applied in $X = 0$) reads, respectively,

$$G_m(X,T) = \frac{1}{\sqrt{\pi T}} e^{-(X^2/\pi T+T)}, \quad (11)$$
and

\[ H_m(X, T) = \int_0^T \frac{1}{\sqrt{\pi T'}} e^{-\frac{X^2}{4T'}} dT', \]  

(12)

We emphasize that in this standard case the Green function \( G_m(X, T) \) is equal to the Green function for the Cauchy problem, name it \( G_c(X, T) \), for an infinite cable up to constant coefficients.

The motion of ions along the nerve cells is conditioned by this model, that predicts a mean square displacement of diffusing ions that scales linearly with time. By the way significative deviations from linear behaviour have been measured by experiments. A relevant medical and biological example is the anomalous subdiffusion in neuronal dendritic spines. Particularly appropriate systems are spiny Purkinje cell dendrites characterized by both spiny and not spiny branches. Spiny branches are in fact characterized by subdiffusive dynamics, while not spiny branches are not. The spatial variance of a diffusing inert tracer (concentration of) in spiny branches evolves as a sub-linear power law of time, and the diffusion with smaller values of the power exponent is associated to higher spine density [22], as spines behave as a trap for the diffusing molecules.

Anomalous subdiffusion can be modelled in several ways introducing some fractional component into the classical cable model. The fractional cable model developed in this section is defined by replacing the first order time derivative in Eq.(2) with a fractional derivative of order \( \alpha \in (0, 1) \) of Caputo type [4], [21].

\[ \frac{\partial^2 V_m(X, T)}{\partial X^2} - \frac{\partial^\alpha V_m(X, T)}{\partial T^\alpha} - V_m(X, T) = 0. \]  

(13)

The solutions of the most relevant boundary problems (Signal Problem, Cauchy Problem, Second Kind Boundary Problem [8]) are explicitly calculated in integral form containing Wright functions. Thanks to the variability of the parameter \( \alpha \), the corresponding solutions are expected to better describe the qualitative behaviour of the membrane potential observed in experiments respect to the standard case \( \alpha = 1 \).

From a mathematical point of view this model is a simple extension to frac-
tional behaviour of the Neuronal Cable Model and it turns to be in some special
cases equivalent to the equation developed in a relevant study [6], which has
been derived from a modified Nernst-Planck equation, with diffusion constant
replaced by fractional derivatives of Riemann-Liouville type. Other studies con-
sider similar approaches [6], [10], [9], [11], [16], often concentrating on the Initial
Value Problem (Cauchy Problem). We will see that beside the apparent sim-
plcity our approach allows to reproduce at least qualitatively the main charac-
teristics observed in experiments [19], [7], [3], [24]. Further generalizations of this
model introducing a second fractional time derivative to the shift term could be
analysed in future, to refine the biological relevance of the model. The solution
for the Signal Problem, derived by the authors of the present work, has been
presented and accepted for publication in AIP Conference Proceedings [25] and
is reported here for sake of completeness.

2. Solution of the Signalling Problem via Laplace Transform

The solution of the Signalling Problem can be derived via Laplace Transform,
however the inversion of the LT solution for Eq. (13) requires special effort
because of the term $V_m(X,T)$.

When this term is not present, the resulting equation is the well known time
fractional diffusion equation:

$$\frac{\partial^2 V_m^*(X,T)}{\partial X^2} - \frac{\partial^\alpha V_m^*(X,T)}{\partial T^\alpha} = 0.$$  \hspace{1cm} (14)

for which the solutions of the corresponding Cauchy and signalling problems
have been derived in the 1990’s by Mainardi in terms of 2 auxiliary Wright
functions (of the second type) [13, 14]. Specifically for the signalling problem
the general solution provided by Mainardi in integral convolution form reads

$$V_m^*(X,T) = \int_0^T g(T-T') G_{\alpha,s}^*(X,T') dT', \quad G_{\alpha,s}^*(X,T) = \frac{1}{T} W_{-\alpha/2,0} \left(-X/T^{\alpha/2}\right),$$  \hspace{1cm} (15)

where $G_{\alpha,s}^*(X,T)$ denotes the Green function of the signalling problem of the
fractional time diffusion equation (Eq.14) and $W_{-\alpha/2,0}(\cdot)$ is a particular case of
the transcendental function known as Wright function

\[ W_{\lambda,\mu}(z) := \sum_{n=0}^{\infty} \frac{z^n}{n! \Gamma[\lambda n + \mu]}, \quad \lambda > -1, \mu \geq 0. \]  \hspace{1cm} (16)

This function, entire in the complex plane, is discussed extensively in the Appendix F of Mainardi’s book \[15\] where the interested reader can find the following relevant Laplace transform pairs, rigorously derived by Stanković \[23\]:

\[ t^{\mu-1} W_{-\nu,\mu} \left(-\frac{x}{t^{\nu}}\right) \div s^{-\mu} \exp \left(-xs^{\nu}\right), \quad 0 \leq \nu < 1, \mu > 0. \]  \hspace{1cm} (17)

Here we have adopted an obvious notation to denote the juxtaposition of a locally integrable function of time \( t \) with its Laplace transform in \( s \) with \( x \) a positive parameter. It is worth to recall the distinction of the Wright functions in first type (\( \lambda \geq 0 \)) and second type (\( -1 < \lambda \leq 0 \)) and, among the latter ones, the relevance of the two auxiliary functions introduced in \[13\]:

\[ F_{\nu}(z) = W_{-\nu,0}(-z), \quad M_{\nu}(z) = W_{-\nu,1-\nu}(-z), \quad 0 < \nu < 1, \]  \hspace{1cm} (18)

inter-related as \( F_{\nu}(z) = \nu z M_{\nu}(z) \). Indeed the relevance of both the Wright functions has been outlined by several authors in diffusion and stochastic processes. Particular attention is due to the \( M \)-Wright function (also referred to as the Mainardi function in \[21\]) that, since for \( \nu = 1/2 \) reduces to \( \exp \left(-z^2/4\right)/\sqrt{\pi} \), is considered a suitable generalization of the Gaussian density, see \[20\] and references therein.

Then the Green function for the signalling problem of the time fractional diffusion equation (Eq\[14\]) can be written in the original form provided in \[13\] as

\[ G_{\alpha,s}(X,T) = \frac{1}{T} F_{\alpha/2} \left( X/T^{\alpha/2} \right) = \frac{\alpha}{2} \frac{X}{T^{\alpha/2+1}} M_{\alpha/2} \left( X/T^{\alpha/2} \right), \]  \hspace{1cm} (19)

where the superscript * is added to distinguish the time fractional diffusion equation from our fractional cable equation, both depending on the order \( \alpha \in (0,1). \)

Applying the Laplace transform to Eq\[13\] with the boundary conditions required by the signalling problem, that is \( V_m(X,0^+) = 0, V_m(0,T) = g(T) \), we
have:

\[(s^\alpha + 1)\tilde{V}_m(X, s) - \frac{\partial^2 \tilde{V}_m(X, s)}{\partial X^2} = 0,\]  

(20)

which is a second order equation in the variable \(X\) with solution:

\[\tilde{V}_m(X, s) = \tilde{g}(s)e^{-\sqrt{(s^\alpha + 1)}X}.\]  

(21)

Because of the shift constant in the square root of the Laplace transform in Eq.(21) the inversion is no longer straightforward with the Wright functions as it is in the time fractional diffusion equation (Eq.(14)). Consequently, we have overcome this difficulty recurring to the application of the Efros theorem [5] that generalizes the well known convolution theorem for Laplace transforms.

For sake of convenience let us hereafter recall this theorem, usually not so well-known in the literature. The Efros theorem states that if we can write a Laplace transform \(\tilde{f}(s)\) as:

\[\tilde{f}(s) = \phi(s) \cdot \tilde{F}(\psi(s)),\]  

(22)

where the function \(\tilde{F}(s)\) has a known inverse Laplace transform \(F(T)\), the inverse Laplace transform can be written in the form:

\[f(T) = \int_0^\infty F(\tau)G(\tau,T)d\tau\]  

(23)

where:

\[G(\tau,T) = \tilde{G}(\tau,s)e^{-\tau\psi(s)}\]  

(24)

In Eq.(21) LT solution of our signalling problem, we thus have:

\[\phi(s) = \tilde{g}(s), \quad \psi(s) = s^\alpha,\]  

(25)

and

\[\tilde{F}(s)|_X = e^{-X\sqrt{s+1}}.\]  

(26)

Then, having \(\tilde{G}(\tau,s) = \tilde{g}(s)e^{-\tau s^\alpha}\), thanks to the standard convolution theorem of Laplace transforms, we obtain:

\[G(\tau,T) = \int_0^T \frac{g(T - T')}{T'}W_{-\alpha,0}(\tau/T'^\alpha)dT'\]  

(27)
where $W_{-\alpha,0}$ is the F-Wright function, and

$$F(T)|_X = \frac{X}{\sqrt{4\pi T^3}} e^{-\left(\frac{X^2}{4T} + T\right)}$$  \hspace{1cm} (28)

is the solution in Eq[5] of the standard cable equation (Eq[2]).

Then, the general solution for the signal problem can be written in terms of known functions:

$$V_m(X, T) = \int_0^\infty \frac{X}{\sqrt{4\pi T^3}} e^{-\left(\frac{X^2}{4T} + T\right)} \left[ \int_0^T \frac{g(T - T')}{T'} W_{-\alpha,0}(-\tau/T'^\alpha) dT' \right] d\tau$$

$$V_m(X, T) = \int_0^T g(T - T') \left[ \int_0^\infty \frac{X}{\sqrt{4\pi T'^3}} e^{-\left(\frac{X^2}{4T'} + T'\right)} \frac{1}{T'} F_\alpha\left(\frac{\tau}{T'^\alpha}\right) d\tau \right] dT' \hspace{1cm} (29)$$

Substituting $g(T) = \delta(T)$ in the general solution in Eq[29] we obtain the Green function for the fractional model (Eq[13], shown in Fig[11])

$$V_m(X, T) := G_{\alpha,s}(X, T) = \int_0^\infty G_s(X, \tau) \frac{1}{T^{\alpha}} M_\alpha\left(\tau/T^{\alpha}\right) d\tau$$

$$V_m(X, T) := H_{\alpha,s}(X, T) = \int_0^\infty G_s(X, \tau) G^{*}_{2\alpha,s}(\tau, T) d\tau$$  \hspace{1cm} (30)

When $g(T) = \theta(T)$ we obtain the step response of our fractional cable equation

$$V_m(X, T) := H_{\alpha,s}(X, T) = \int_0^\infty G_s(X, \tau) \left[ \int_0^\tau G^{*}_{2\alpha,s}(\tau, T') dT' \right] d\tau$$

$$V_m(X, T) := H_{\alpha,s}(X, T) = \int_0^\infty G_s(X, \tau) H^{*}_{2\alpha,s}(\tau, T) d\tau$$

After some manipulations including the change of variable $z = \tau/T'^\alpha$ and integrating by parts after using the recurrence relation of Wright functions:

$$\frac{dW_{\alpha,\mu}(z)}{dz} = W_{\lambda,\lambda+\mu}(z)$$

and the relation between the auxiliary functions: $F_\nu(z) = \nu z M_\nu(z)$ we may rewrite the step-response solution as:

$$V_m(X, T) := H_{\alpha,s}(X, T) = \int_0^\infty H_s(X, \tau) \cdot \frac{1}{T^{\alpha}} M_\alpha\left(\frac{\tau}{T^{\alpha}}\right) d\tau$$

$$V_m(X, T) := H_{\alpha,s}(X, T) = \int_0^\infty H_s(X, \tau) G^{*}_{2\alpha,c}(\tau, T) d\tau$$

\hspace{8cm} (31)  \hspace{8cm} (32)  \hspace{8cm} (33)  \hspace{8cm} (34)  \hspace{8cm} (35)
where $\mathcal{H}_{\alpha,s}(X,T)$ is the step response function for the standard cable model and $G^{2\alpha,c}_{\tau,T}(\tau,T)$ is the fundamental solution of the time fractional diffusion equation for the Cauchy Problem. The same expression can easier be derived by direct application of the Efros theorem and is plotted in Fig. 2.

Figure 1: Green function for Signal Problem is calculated and plotted for $X = 1$ as function of time $T$ (left panel) and for $T = 1$ as function of $X$ (right panel). Several values of parameter $\alpha$ are compared: 0.25, 0.5, 0.75, 1.

Figure 2: Step response function for Signal Problem is calculated and plotted for $X = 1$ as function of time $T$ (left panel) and for $T = 1$ as function of $X$ (right panel). Several values of parameter $\alpha$ are compared: 0.25, 0.5, 0.75, 1.

3. The Green function for the Cauchy Problem

Consider an infinite cable with boundary conditions $V_m(\pm\infty, T) = 0$ and initial condition $V_m(X, 0) = f(X)$. The general solution of the Cauchy problem
is related to the Green function $G_{\alpha,c}(X,T)$ through the following relation:

$$V_m(X,T) = \int_{-\infty}^{+\infty} f(x - \xi)G_{\alpha,c}(\xi,T)d\xi.$$  \hfill (36)

$G_{\alpha,c}(X,T)$ can be derived via Laplace Transform:

$$(s^\alpha + 1)\tilde{G}_{\alpha,c}(X,s) - \frac{\partial^2 \tilde{G}_{\alpha,c}}{\partial X^2} = \delta(X)s^{\alpha - 1},$$  \hfill (37)

boundary conditions imposes:

$$\tilde{G}_{\alpha,c}(X,s) = \begin{cases} 
  c_1(s)e^{-X\sqrt{s^{\alpha} + 1}}, & \text{if } X > 0 \\
  c_2(s)e^{X\sqrt{s^{\alpha} + 1}}, & \text{if } X < 0
\end{cases}$$  \hfill (38)

Imposing $\tilde{G}_{\alpha,c}(0^-,s) = \tilde{G}_{\alpha,c}(0^+,s)$ leads to $c_1(s) = c_2(s)$. Integrating Eq.(33) over $X$ from $0^-$ to $0^+$ we have:

$$\frac{\partial \tilde{G}_{\alpha,c}(0^+,s)}{\partial X} - \frac{\partial \tilde{G}_{\alpha,c}(0^-,s)}{\partial X} = -s^{\alpha - 1}$$  \hfill (39)

the coefficients result:

$$c_1(s) = c_2(s) = \frac{1}{2s^{1-\alpha}\sqrt{s^\alpha + 1}}$$  \hfill (40)

the resulting LT of the Green function reads:

$$\tilde{G}_{\alpha,c}(X,s) = \frac{1}{2s^{1-\alpha}\sqrt{s^\alpha + 1}}e^{-X\sqrt{s^{\alpha} + 1}}$$  \hfill (41)

The inversion can be easily performed for $X > 0$, thanks again to the Efros theorem, and extended by symmetry respect to the $X$-axes for $X < 0$.

Let’s consider $\phi(s) = \frac{1}{s^{1-\alpha}}$, $\psi(s) = s^\alpha$, following the theorem we may set $G(\tau,s) = \frac{1}{s^{1-\alpha}}e^{-\tau s^\alpha}$ and $F(X,s) = \frac{1}{2\sqrt{s^\alpha + 1}}e^{-X\sqrt{s^\alpha + 1}}$, that have known inverse LT:

$$F(X,T) = \frac{1}{\sqrt{4\pi T}}e^{-\frac{X^2}{4T}}$$  \hfill (42)

and

$$G(\tau,T) = \frac{1}{T^\alpha}W_{-\alpha,1-\alpha}(-\tau/T^\alpha) = \frac{1}{T^\alpha}M_{\alpha}(\tau/T^\alpha)$$  \hfill (43)

The inverse LT for the Green function is plotted in Fig.3 and reads:

$$G_{\alpha,c}(X,T) = \int_0^{\infty} \frac{1}{\sqrt{4\pi \tau}}e^{-\frac{X^2}{4\tau} + \tau} \frac{1}{T^\alpha}M_{\alpha}(\tau/T^\alpha)d\tau$$

$$= \int_0^{\infty} G_c(X,\tau)G^{*}_{2\alpha,c}(\tau,T)d\tau$$  \hfill (44)
Figure 3: Green function for Cauchy Problem is calculated and plotted for $X = 1$ as function of time $T$ (left panel) and for $T = 1$ as function of $X$ (right panel). Several values of parameter $\alpha$ are compared: 0.25, 0.5, 0.75, 1.

4. Response to injected current

An interesting biological problem is to consider an injected current in the system. Transmembrane potential is related to the transmembrane current through the relation $-I = \frac{\partial^2 V_m(X,T)}{\partial X^2}$, where the minus sign is due to the direction of the current, in this case flowing inside the cell. Let’s consider a singular point injected current in $X = 0$, it takes the form $I(X, T) = I_0 \delta(X)f(T)$. Integrating from $0^-$ to $0^+$ we obtain the relation

$$-I_0 f(T) = \frac{\partial V_m(X, T)}{\partial X}|_{X=0^+} - \frac{\partial V_m(X, T)}{\partial X}|_{X=0^-} \quad (45)$$

We recall the LT for the semi-infinite cable for an initially undisturbed cable:

$$\tilde{V}_m(X, s) = \tilde{V}_m(0, s)e^{-X\sqrt{s^\alpha + 1}}. \quad (46)$$

At the boundary condition we have:

$$I_0 \tilde{f}(s) = -\frac{\partial \tilde{V}_m(X, s)}{\partial X}|_{X=0^+}, \quad (47)$$

if we consider an impulse injection of current in $X = 0$ we have $I_0 \delta(T) = -\frac{\partial \tilde{V}_m(X, T)}{\partial X}|_{X=0^+}$. Applying this condition to the LT we obtain:

$$\tilde{V}_m(0^+, s) = \frac{I_0}{\sqrt{s^\alpha + 1}} \quad (48)$$
leading to the following Laplace Transformed solution:

\[ \tilde{G}_{\alpha,m}(X,s) = \frac{I_0}{\sqrt{s^\alpha + 1}} e^{-X\sqrt{s^\alpha + 1}} \] (49)

According to the previous derivations it is then straightforward that the inverse LT takes the form:

\[ G_{\alpha,m}(X,T) = \int_0^\infty \frac{I_0}{\sqrt{\pi T}} e^{-\left(\frac{X^2}{4T}\right)} \frac{1}{T} W_{-\alpha,0}(-\tau/T^\alpha) d\tau \]

\[ = \int_0^\infty \tilde{G}_{m}(X,\tau) \tilde{G}_{2\alpha,c}^*(\tau,T) d\tau, \] (50)

represented in Fig.4.

For a generic boundary \( I_0 \tilde{f}(s) \) we obtain:

\[ \tilde{V}_m(X,s) = \frac{I_0 f(s)}{\sqrt{s^\alpha + 1}} e^{-X\sqrt{s^\alpha + 1}} \] (51)

The general solution becomes:

\[ V_m(X,T) = \int_0^T f(T-T')G_{\alpha,m}(X,T')dT' \] (52)

The solution is symmetric respect to \( X \), the problem can be then extended to the infinite cable introducing a factor \( 1/2 \): \( G_{\alpha,m}^\infty(X,T) = \frac{1}{2} G_{\alpha,m}(X,T) \)

The extension to the infinite cable case admits also the following generalization, current injection in \( X_0 \neq 0 \) is equivalent to shift the cable of the same value \( X_0 \), then:

\[ V_{X_0,m}^\infty(X,T) = \int_0^T f(T-T')G_{\alpha,m}^\infty(X-X_0,T')dT' \] (53)

When the injected current is a step function we obtain the following LT solution:

\[ \tilde{H}_{\alpha,m}(X,s) = \frac{I_0}{s\sqrt{s^\alpha + 1}} e^{-X\sqrt{s^\alpha + 1}} = \frac{I_0}{s^{1-\alpha}s^\alpha\sqrt{s^\alpha + 1}} e^{-X\sqrt{s^\alpha + 1}} \] (54)

considering \( \phi(s) = \frac{1}{s^{1-\alpha}} \), \( \psi(s) = s^\alpha \) we have \( G(\tau,s) = \frac{1}{s^{1-\alpha}} e^{-\tau s^\alpha} \) and \( F(X,s) = \frac{1}{s\sqrt{s^\alpha + 1}} e^{-X\sqrt{s^\alpha + 1}} \), that have known inverse LT Eq.53 can be simplified to:

\[ H_{\alpha,m}(X,T) = \int_0^\infty H_{m}(X,\tau) \frac{1}{T^\alpha} M_0(\tau/T^\alpha) d\tau \]

\[ = \int_0^\infty H_{m}(X,\tau) \tilde{G}_{2\alpha,c}^*(\tau,T) d\tau, \] (55)

which is shown in Fig.5
5. Conclusions

The cable model, fractional or linear, is used to describe subthreshold potentials, or passive potentials, associated to dendritic processes in neurons. The travelling potential is summed up in the center of the cell, called soma, and an action potential is produced when a threshold is exceeded. Anomalous regimes of diffusion can then have a deep impact on the communication strength.

Diffusion results more anomalous, i.e. the fractional exponent $\alpha$ decreases, with increasing spine density [22]. Decreasing spine density is characteristic of
aging [7, 8], pathologies as neurological disorders [19] and Down’s syndrome [24],
then subdiffusive regimes are in some sense associated to a healthy condition.
It has been suggested that increasing spine density should serve to compensate
time delay of postsynaptic potentials along dendrites and to reduce their long
time temporal attenuation [6].

Looking at our plotted solutions for the fractional cable equation when an
impulsive potential is applied at the accessible end it can be noted from Fig.1
that peak high decreases more rapidly with decreasing $\alpha$ at early times, vicev-
ersa is less suppressed at longer times, and the cross over time increases with
decreasing $\alpha$. Looking at the potential versus time it can also be noted that
potential functions associated to lower $\alpha$ last for longer time at appreciable
intensity and arrive faster at early times with respect to the normal diffusion
case ($\alpha = 1$). By the way, when a constant potential is applied at the acces-
sible end we note from Fig.2 that the exponential suppression of the potential
along the dendrite is reduced for high $X$ values with respect to normal diffusion.
Instead for small $X$ the potential results just slightly more suppressed in the
sub-diffusion process. These behaviours can be noticed also for the other cases
in Fig.3 and Fig.4-5.

From a mathematical point of view the Efros theorem extends the concept
of convolution as an integral form that is consistent with a subordination-type
integral. However such integral form does not necessary connote a subordinated
process, as it has been shown in literature for ggBM [18] and in a more extended
way in [17], but could also be interpreted as a consequence of the random nature
of the media in which particles are diffusing. This model can be also read as
a generalization of time fractional diffusion processes where mass is not con-
served due to leakage. This approach naturally recover the solution for the time
fractional case in the limit in which the leakage is put to zero in the integral
forms.

In conclusion the presented fractional cable model satisfies the main biolog-
ical features of the dendritic cell signalling problem. With respect to models
solved as Cauchy problem, our approach could include specific time dependent
boundary conditions, which will allow to reconstruct with accuracy the expected signal at the soma if the model will result capable to predict real data behaviour. Furthermore the solutions can be computed directly, i.e. calculating the integral associated, as well as by Laplace Transform inversion \cite{1} without any remarkable issue.

6. Acknowledgements

The work of F. M. has been carried out in the framework of the activities of the National Group of Mathematical Physics (INdAM-GNFM). The authors are indebted to the Interdepartmental Center ”Luigi Galvani” for integrated studies of Bioinformatics, Biophysics and Biocomplexity of the University of Bologna for partial support.

References

References

[1] Abate, J. and Ward, W. (2006). A unified framework for numerically inverting laplace transforms. *INFORMS J. on Computing*, 18(4):408–421.

[2] D.Johnston and S.M.S.Wu (1994). *Foundations of Cellular Neurophysiology (Bradford Books)*. Bradford Books. The MIT Press, 1 edition.

[3] Duan, H. (2003). Age-related dendritic and spine changes in corticocortically projecting neurons in Macaque monkeys. *Cerebral Cortex*, 13.

[4] Gorenflo, R. and Mainardi, F. (1997). *Fractional Calculus: Integral and Differential Equations of Fractional Order* in A. Carpinteri and F. Mainardi (Editors), Vol. 378. pages 223–276. Springer-Verlag, Wien. CISM Courses and Lecture Notes, (ISBN 3-211-82913-X) [E-print http://arxiv.org/abs/0805.3823].

[5] Graf, U. (2004). *Applied Laplace Transforms and z-Transforms for Scientists and Engineers*. Springer.
[6] Henry, B., Langlands, T., and Wearne, S. (2008). Fractional cable models for spiny neuronal dendrites. *Phys. Rev. Lett.*, 100:128103/1–3.

[7] Jacobs, B., Driscoll, L., and Schall, M. (1997). Life-span dendritic and spine changes in areas 10 and 18 of human cortex: A quantitative golgi study. *The Journal of Comparative Neurology*, 386.

[8] Kevorkian, J. (2000). *Partial Differential Equations: Analytical Solution Techniques*. Texts in Applied Mathematics 35. Springer New York.

[9] Langlands, T., Henry, B., and Wearne, S. (2011). Fractional cable equation models for anomalous electrodiffusion in nerve cells: Finite domain solutions. *SIAM Journal on Applied Mathematics*, 71.

[10] Langlands, T., Henry, B. I., and Wearne, S. (2009). Fractional cable equation models for anomalous electrodiffusion in nerve cells: infinite domain solutions. *Journal of Mathematical Biology*, 59.

[11] Liu, F., Yang, Q., and Turner, I. (2011). Two new implicit numerical methods for the fractional cable equation. *Journal of Computational and Nonlinear Dynamics*, 6.

[12] Magin, R. (2006). *Fractional Calculus in Bioengineering*. Begell House Publishers.

[13] Mainardi, F. (1996). Fractional relaxation-oscillation and fractional diffusion-wave phenomena. *Chaos, Solitons and Fractals*, 7:1461–1477.

[14] Mainardi, F. (1997). *Fractional Calculus: Some Basic problems in Continuum and Statistical Mechanics*, in A. Carpinteri and F. Mainardi (Editors), Vol. 378, pages 291–348. Springer-Verlag, Wien. CISM Courses and Lecture Notes.(ISBN 3-211-82913-X) [E-print http://arxiv.org/abs/1201.0863] .

[15] Mainardi, F. (2010). *Fractional Calculus and Waves in Linear Viscoelasticity*. Imperial College Press, London, 1st edition.
[16] Moaddy, K., Radwan, A. G., Salama, K. N., Momani, S., and Hashim, I. (2012). The fractional-order modeling and synchronization of electrically coupled neuron systems. *Comput. Math. Appl.*, 64(10):3329–3339.

[17] Molina-Garca, Daniel; Pham, T. M. P. M. C. P. G. (2016). Fractional kinetics emerging from ergodicity breaking in random media. *Physical Review E*, 94.

[18] Mura, A; Pagnini, G. (2008). Characterizations and simulations of a class of stochastic processes to model anomalous diffusion. *Journal of Physics A Mathematical and Theoretical*, 41.

[19] Nimchinsky, E. A., Sabatini, B. L., and Svoboda, K. (2002). Structure and function of dendritic spines. *Annual Review of Physiology*, 64.

[20] Pagnini, G. (2013). The M-Wright function as a generalization of the Gaussian density for fractional diffusion processes. *Fract. Calc. Appl. Anal.*, 16.

[21] Podlubny, I. (1999). *Fractional Differential Equations*. Mathematics in Science and Engineering 198. Academic Press, San Diego, 1st edition.

[22] Santamaria, F., Wils, S., Schutter, E. D., and Augustine, G. J. (2006). Anomalous diffusion in purkinje cell dendrites caused by spines. *Neuron*, 52.

[23] Stanković, B. On the function of E.M. Wright. *Publ. de l’InstitutMathématique, Beograd, Nouvelle Sér.*, 10:113–124.

[24] Suetsugu, M. and Mehraein, P. (1980). Spine distribution along the apical dendrites of the pyramidal neurons in Down’s syndrome. *Acta Neuropathologica*, 50.

[25] S.Vitali and F.Mainardi (2008). Fractional cable model for signal conduction in spiny neuronal dendrites. *AIP Conference Proceedings*, Accepted.