1-1-2021

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Results in Physics 21 (2021) 103809

Contents lists available at ScienceDirect

Results in Physics

journal homepage: www.elsevier.com/locate/rinp

Explicit tight frames for simulating a new system of fractional nonlinear partial differential equation model of Alzheimer disease

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ARTICLE INFO

Keywords:
Time fractional differential equation
Caputo's fractional derivative
Alzheimer disease
Mathematical modeling
Drug treatment
Tight frames

ABSTRACT

This paper is devoted to develop a new mathematical model for Alzheimer disease based on a system of fractional-order partial differential equations. The system of Alzheimer disease includes neurons, astrocytes, microglias and peripheral macrophages, as well as amyloid β aggregation and hyperphosphorylated tau proteins. We consider the Caputo fractional derivative definition to analyze the formulated system by simulating the effect of drugs that either failed or currently in clinical trials. To simulate the model, we use tight frame (framelet) systems generated using the unitaryand oblique extension principle. According to the simulation results, and based on using such new direction of fractional modeling, the progression of Alzheimer disease and its consequences will be slowing down. Which may give clinical insights on intervention measures against the disease and its effective therapies.

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease that causes brain cells to waste away which leads to protein aggregation, where the neurodegeneration are only partially understood. It is known as the most common form of dementia and mortality in the elderly [1,2]. Noticing that, the increasing number of older adults afflicted with AD, is causing many challenges for the global health community. For example, the prevalence of AD worldwide in 2006 was 26.12 million, in 2019 it is estimated that 46.8 million people suffer from AD, and by 2030 the prevalence estimated to be 74.7 million people [3], and approximately it is expected that this number to be increased by 1.2% in 2050 [4] taking into account the huge amount of cost of caring for AD adults afflicted. For example, in the United States of America the cost was approximately \$290 billion in 2019, but the costs extend to many other reasons such as the negative mental and physical health outcomes [5]. Given these circumstances (among others), developing models that describe the dynamics of such disease is essential. Consequently, there is an immediate call for effective and efficient models that be able to provide some insights for effective description of the dynamics of AD including neurons, astrocytes, therapies and many other factors for the disease.

Most recently, many scientists have applied fractional derivatives using wavelets, framelets and many other systems on many scientific and disease models in order to achieve a better matched with the reality and dynamics of these models rather than using the classical ordinary differential equations [6–15,17–37]. It is well-known that the fractional order options, especially with the Caputo fractional derivative, are more suitable to describe the medical phenomena than the classical and integer order [38–40]. This is also due to the fact that Caputo fractional definition describe the modeling of the non-local issues more efficiently.

The main aim of this work is to extend the AD mathematical model presented in [41], that is initially formulated based on integer-order derivative, by applying the Caputo fractional operator derivative. There are many advantages of using such derivative operator in applications. In future, we intended to study this AD model in other sense such as Atangana-Baleanu and Caputo-Fabrizio and compare their differences with the Caputo derivative in order to investigate which one is more appropriate and reliable for describing such model.

Preliminaries and notations

Let us introduce some definitions and notations of tight frames and fractional calculus needed through the paper. An $L^2(\mathbb{R})$-function is a function maps $\mathbb{R}$ to itself such that

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https://doi.org/10.1016/j.rinp.2020.103809
Received 18 August 2020; Received in revised form 26 December 2020; Accepted 30 December 2020
Available online 10 January 2021

$$\| f\|^2_{L^2(\mathbb{R})} = \left(\int_{\mathbb{R}} |f\left(x\right)|^2\right),$$

exists and finite.

The Fourier transform of a function $g \in L_1(\mathbb{R})$ (can be extended to $L_2(\mathbb{R})$) is defined to be

$$\mathscr{F}\left(g\right)\left(\omega\right) = \widehat{g}\left(\omega\right) = \int_{\mathbb{R}} g\left(x\right) e^{-i\omega x} dx, \omega \in \mathbb{R},$$

and the Fourier series of a sequence $a \in \ell_2(\mathbb{Z})$ is defined by

$$\mathscr{F}\left(h\right)\left(\omega\right) = \widehat{h}\left(\omega\right) = \sum_{k\in\mathbb{Z}} a\left[k\right] e^{-i\omega k}, \quad \omega \in \mathbb{R}.$$

Definition 0.1. A sequence of functions $\{g_k \in L^2(\mathbb{R}), k = 1, \dots, \infty\}$ is called a *frame* of $L^2(\mathbb{R})$ if there exist a positive constants T_1, T_2 such that,

$$T_1 \parallel g\|^2 \leqslant \sum_{k=1}^{\infty} |\langle g, g_k\rangle|^2 \leqslant T_2 \parallel g\|^2, \quad \forall g \in L^2\left(\mathbb{R}\right).$$

The constants T_1, T_2 are called frame bounds. A frame in Definition 0.1 is called *Parseval* (*tight*) if it is possible to have $T_1 = T_2$, and $T_1 = T_2 = 1$, respectively.

In applications, it is recommend to use a non-negative functions to simulate the problem. B-splines are an example of non-negative functions and have many mathematical features such as symmetry and refinability. The B-spline B_m of order m is defined by the following relation,

$$B_m = B_{m-1} {}^* B_1 = \int_{(0,1]} B_{m-1}\left(\cdot - x\right) dx, \quad m = 1, \dots, \infty,$$

where

$$B_1 = \chi_{(0,1]},$$

is defined to be the indicator function over the interval $[0, 1)$.

We say a function g has N vanishing moments if

$$\int t^m g\left(t\right) dt = 0, \quad \text{for} \quad m = 0, 1, \dots, N-1.$$

In this paper, we use the B-splines as refinable functions to construct the tight frame systems in order to simulate thenew formulated AD model.

For $g \in L^2(\mathbb{R})$, we define the dilation operator D by $Dg(x) = \sqrt{2}g(2x)$, and the translation operator T by $T_k g(x) = g(x-k)$ for $k \in \mathbb{Z}$. A compactly supported square-integrable function ϕ is called refinable if we have

$$\phi\left(x\right) = 2\sum_{k\in\mathbb{Z}} a_0\left[k\right]\phi\left(2x - k\right),$$

where $a_0[k]$ is finitely supported sequence.

Let $\Psi = \{\psi_\ell\}_{\ell=1}^r$ be a set of square integrable functions such that

$$\psi^\ell = 2\sum_{k\in\mathbb{Z}} b^\ell\left[k\right]\phi\left(2\cdot - k\right),$$

where $\{b_\ell[k], k \in \mathbb{Z}\}_{\ell=1}^r$ is a finitely supported sequence. To simulate the non-linear system of partial differential equations PDEs for the AD in this work we need to construct tight frame systems of the form of $X(\Psi)$, where

$$X(\Psi) = \left\{\psi^\ell_{j,k} = D^j T_k \psi^\ell; \quad j,\ k \in \mathbb{Z}, \quad \ell = 1, \dots, r\right\}.$$

The system is generated using the well-known unitary and oblique extension principles [42,43].

Theorem 0.2. [[42]] *For a given refinable ϕ, the system $X(\Psi)$ is a tight frame for the space $L^2(\mathbb{R})$ if*

$$\sum_{\ell=0}^{r} \sum_{k\in\mathbb{Z}} \overline{b^\ell[k]} b^\ell\left[k - q\right] = \delta_{0,p},$$

and

$$\sum_{\ell=0}^{r} \sum_{k\in\mathbb{Z}} (-1)^{k-q} \overline{b^\ell[k]} b^\ell\left[k - q\right] = 0,$$

hold for all $q \in \mathbb{Z}$, where $\delta_{0,q}$ is the Kronecker delta function. The oblique extension principle presented is a generalization of the unitary extension principle and to have such extension, it is require to have some required constraints on $a[k]$. That is, for some trigonometric function $\widehat{\Theta}$, for $\sigma \in \{0, 1\}$,

$$\widehat{\Theta}\left(\cdot\right)|\widehat{\phi}\left(0\right)|^2 = 1,$$
$$\sum_{\ell\in E} \widehat{b}^\ell\left(\cdot\big/2 + \pi\sigma\right)\overline{\widehat{b}^\ell\left(\xi/2\right)} = \Theta\left(\xi\big/2\right)\delta_\sigma - \widehat{\Theta}\left(\xi\right)\widehat{a}\left(\xi\big/2 + \pi\sigma\right).$$

Note that, according to Definition 0.1 and Theorem 0.2, we have the following *tight frame* expansion,

$$g = \sum_{\ell=1}^{r} \sum_{j,k\in\mathbb{Z}} \left\langle g, \psi^\ell_{j,k}\right\rangle \psi^\ell_{j,k}. \tag{2.1}$$

Let us now construct some tight frame systems using the above principles. Define the function sgn as

$$\operatorname{sgn}\left(x\right) = \frac{x}{|x|}, \quad x \neq 0.$$

Example 0.1. Applying the OEP and considering the B-spline of order two, B_2, we have

$$\psi_1\left(x\right) = \frac{1}{\sqrt{2}}\left(-|x-1| + |x+1| - 2\left|x + \frac{1}{2}\right| + \operatorname{sgn}\left(\frac{1}{2} - x\right) + 2x\ \operatorname{sgn}\left(x - \frac{1}{2}\right)\right),$$
$$\psi_1\left(x\right) = \frac{1}{2}\left(-6|x| - |x+1| + 4\left|x - \frac{1}{2}\right| + 2|2x+1| + x\ \operatorname{sgn}\left(1 - x\right) + \operatorname{sgn}\left(x - 1\right)\right).$$

Then, the system $X(\Psi)$ forms a tight frame for $L^2(\mathbb{R})$.

Example 0.2. For the B-spline of order four, B_4, and again by applying the notion of the OEP we get

$$\psi_1\left(x\right)=\frac{1}{24}\left(-4|x-2|^3+8|x-1|^3-8|x+1|^3+4|x+2|^3+3|2x+1|^3-|2x+3|^3-3|1-2x|^3+|3-2x|^3\right),$$
$$\psi_2\left(x\right)=\frac{1}{4\sqrt{6}}\left(2|x-2|^3+8|x-1|^3-20|x|^3+8|x+1|^3+2|x+2|^3+|2x+1|^3-|2x+3|^3+|1-2x|^3-|3-2x|^3\right),$$
$$\psi_3\left(x\right)=\frac{1}{24}\left(-4|x-2|^3-56|x-1|^3+56|x+1|^3+4|x+2|^3-7|2x+1|^3-3|2x+3|^3+7|1-2x|^3+3|3-2x|^3\right)$$
$$\psi_4\left(x\right)=\frac{-1}{12}\left(-|x-2|^3-28|x-1|^3-70|x|^3-28|x+1|^3-|x+2|^3+7|2x+1|^3+|2x+3|^3+7|1-2x|^3+|3-2x|^3\right).$$

Then, the system $X(\Psi)$ forms a tight frame for $L^2(\mathbb{R})$.

Definition 0.3. For a real-valued function $u(t)$, suppose that $0<q<1$. Let Γ be the Euler gamma function, then:

- The Caputo's fractional order derivative is defined as follows,

$$\mathscr{D}^q u\left(t\right)=\frac{1}{\Gamma(1-q)}\int_0^t\frac{u'(x)}{(t-x)^q}dx.$$

- The associated Riemann–Liouville integral fractional operator is given by,

$$\mathscr{I}^q u\left(t\right)=\frac{1}{\Gamma(q)}\int_0^t\frac{u(x)}{(t-x)^{1-q}}dx.$$

Caputo fractional order mathematical model of AD

Now, we consider the mathematical model of AD using the Caputo fractional order derivative. The model consists of eighteen nonlinear partial differential equations. It is important to notice that to get a matched dimensions on both sides of the AD system we have to change the dimension of each parameter. Therefore, the order of the equations to q, and the dimension of the left-hand side would be $(time)^{-q}$.

$$\mathscr{D}^q A_\beta^i=\left(\lambda_\beta^i\left(1+R\right)-d_{A_\beta^i}A_\beta^i\right)N\Big/N_0 \tag{3.1}$$

$$\mathscr{D}^q A_\beta^0=A_\beta^i\left|\frac{\partial N}{\partial t}\right|+\frac{\lambda_N N}{N_0}+\frac{\lambda_A A}{A_0}-\left(d_{A_\beta^0\widehat{M}}\left(\widehat{M}_1+\widehat{M}_2\theta\right)+d_{A_\beta^0 M}(M_1+M_2\theta)\right)\frac{A_\beta^0}{A_\beta^0+\overline{K}_{A_\beta^0}} \tag{3.2}$$

$$\mathscr{D}^q\tau=\frac{N}{N_0}\left(\lambda_{\tau_0}+\lambda_\tau R-d_\tau\tau\right) \tag{3.3}$$

$$\mathscr{D}^q F_i=\frac{N}{N_0}(\lambda_F\tau-d_{F_i}F_i) \tag{3.4}$$

$$\mathscr{D}^q F_0=F_i\left|\frac{\partial N}{\partial t}\right|-f_{F_o}F_o \tag{3.5}$$

$$\mathscr{D}^q N=\frac{-d_{NF}F_iN}{F_i+K_{F_i}}-\frac{d_{NT}T_\alpha N}{\left(T_\alpha+K_{T_\alpha}\right)\left(K_{I_{10}}+\gamma I_{10}\right)}\Bigg) \tag{3.6}$$

$$\mathscr{D}^q A=\lambda_{AA_\beta^o}A_\beta^o+\lambda_{AT_\alpha}T_\alpha-d_A A. \tag{3.7}$$

$$\mathscr{D}^q N_d=\frac{d_{NF}F_iN}{F_i+K_{F_i}}+\frac{d_{NT}T_\alpha NK_{I_10}}{\left(T_\alpha+K_{T_\alpha}\right)\left(K_{I_{10}}+\gamma I_{10}\right)}-d_{N_dM}(M_1+M_2)\frac{N_d}{N_d+\overline{K}_{N_d}}-d_{N_d\widehat{M}}\left(\widehat{M}_1+\widehat{M}_2\right)\frac{N_d}{N_d+\overline{K}_{N_d}} \tag{3.8, 3.9}$$

$$\mathscr{D}^q A_O=\lambda_{A_O}A_\beta^o-d_{A_O}A_O+D_{A_O}\Delta A_O \tag{3.10}$$

$$\mathscr{D}^q H=\lambda_H N_d-d_H H+D_H\Delta H \tag{3.11}$$

$$\mathscr{D}^q M_1=\left(\frac{M_G^0\lambda_{MF}F_o}{F_o+K_{F_o}}+\frac{M_G^0\lambda_{MA}A_O}{A_O+K_{A_O}}\right)\frac{\beta\epsilon_1}{\beta\epsilon_1+\epsilon_2}-\nabla\cdot\left(M_1\nabla H\right)+\frac{T_\beta M_1\lambda_{M_1T_\beta}}{T_\beta+K_{T_\beta}}-d_{M_1}M_1 \tag{3.12}$$

$$\mathscr{D}^q M_2=\left(\frac{M_G^0\lambda_{MF}F_o}{F_o+K_{F_o}}+\frac{M_G^0\lambda_{MA}A_O}{A_O+K_{A_O}}\right)\frac{\epsilon_2}{\beta\epsilon_1+\epsilon_2}-\nabla\cdot\left(M_2\nabla H\right)+\frac{T_\beta M_2\lambda_{M_2T_\beta}}{T_\beta+K_{T_\beta}}-d_{M_2}M_2 \tag{3.13}$$

$$\mathscr{D}^q\widehat{M}_1=\alpha\left(P\right)\left(M_0-\widehat{M}\right)\frac{\beta\epsilon_1}{\beta\epsilon_1+\epsilon_2}-\nabla\cdot\left(\widehat{M}_1\nabla A_O\right)+\frac{T_\beta\widehat{M}_1\lambda_{\widehat{M}_1T_\beta}}{T_\beta+K_{T_\beta}}-d_{\widehat{M}_1}\widehat{M}_1 \tag{3.14}$$

Table 1
The variables description.

Variable	Description
A_β^i	The amyloid-β within neurons
A_β^0	The extracellular amyloid-β peptides outside neurons
τ	Hyperphosphorylated tau protein
$NFT(F_i)$	The neuronfibrillary tangle within neurons
$NFT(F_0)$	The neuronfibrillary tangle outside neurons
N	Live neurons
A	Astrocytes
$ROS(R)$	Reactive oxygen species
$APP(A_p)$	Amyloid precursor protein
$TNF-\alpha(T_\alpha)$	Tumor necrosis factor alpha
$IL-10(I_{10})$	Interleukin 10
$MG(M_G)$	Microglias
$GSK-3(G)$	Glycogen synthase kinase-type 3
$A\beta O(A_O)$	Amyloid β oligomer (soluble)
$TGF-\beta(T_\beta)$	Transforming growth factor beta
P	MCP-1
M_1	Proinflammatory microglias
$\widehat{M}_1$	Peripheral proinflammatory macrophages
M_2	Anti-inflammatory microglias
$\widehat{M}_2$	Peripheral anti-inflammatory macrophages
N_d	Dead neurons
H	High mobility group box 1 (HMGB1)

$$\mathscr{D}^q\widehat{M}_2=\alpha\left(P\right)\left(M_0-\widehat{M}\right)\frac{\epsilon_2}{\beta\epsilon_1+\epsilon_2}-\nabla\cdot\left(\widehat{M}_2\nabla A_O\right)+\frac{T_\beta\widehat{M}_2\lambda_{\widehat{M}_2T_\beta}}{T_\beta+K_{T_\beta}}-d_{\widehat{M}_2}\widehat{M}_2 \tag{3.15}$$

$$\mathscr{D}^qT_\beta=\lambda_{T_\beta M}M_2+D_{T_\beta}\Delta T_\beta+\lambda_{T_\beta\widehat{M}}\widehat{M}_2-d_{T_\beta}T_\beta \tag{3.16}$$

$$\mathscr{D}^qI_{10}=\lambda_{I_{10}M}M_2+D_{I_{10}}\Delta T_\beta+\lambda_{I_{10}\widehat{M}}\widehat{M}_2-d_{I_{10}}I_{10} \tag{3.17}$$

$$\mathscr{D}^qT_\alpha=\lambda_{T_\alpha M_1}M_1+D_{T_\alpha}\Delta T_\alpha+\lambda_{T_\alpha\widehat{M}_1}\widehat{M}_1-d_{T_\alpha}T_\alpha \tag{3.18}$$

$$\mathscr{D}^qP=\lambda_{PA}A+D_P\Delta P_{\lambda_{PM_2}M_2}-d_PP. \tag{3.19}$$

where

$$\epsilon_1=\frac{T_\alpha}{T_\alpha+K_\alpha},\quad \epsilon_2=\frac{I_{10}}{I_{10}+K_{I_{10}}},\quad \widehat{M}=\widehat{M}_1+\widehat{M}_2,\quad \alpha\left(P\right)=\frac{\alpha P}{P+K_P},$$

and

$$R\left(t\right)=\begin{cases}0.01R_0t, & 0\leqslant t\leqslant 100\\ R_0, & t>100\end{cases}$$

where the description of all variables is presented in Table 1. The AD model is subject to the periodic boundary conditions:

$$A_\beta^O(0,y,t)=A_\beta^O(1,y,t);\quad A_\beta^O(x,0,t)=A_\beta^O(x,1,t);\quad h(0,y,t)=h(1,y,t);\quad h(x,0,t)=h(x,1,t);$$

$$T_\beta(0,y,t)=T_\beta(1,y,t);\quad T_\beta(x,0,t)=T_\beta(x,1,t);\quad I_{10}(0,y,t)=I_{10}(1,y,t);\quad I_{10}(x,0,t)=I_{10}(x,1,t);$$

$$T_\alpha(0,y,t)=T_\alpha(1,y,t);\quad T_\alpha(x,0,t)=T_\alpha(x,1,t);\quad P(0,y,t)=P(1,y,t);\quad P(x,0,t)=P(x,1,t);$$

and the following initial conditions:

$$A_\beta\left(x,y,0\right)=\frac{1}{10^6};\quad A_\beta^O\left(x,y,0\right)=\frac{1}{10^8};\quad \tau\left(x,y,0\right)=\frac{1.37}{10^{10}};\quad F_i\left(x,y,0\right)=\frac{3.36}{10^{10}};\quad F_O\left(x,y,0\right)=\frac{3.36}{10^{11}};$$

$$N\left(x,y,0\right)=0.14;\quad A\left(x,y,0\right)=0.14;\quad M_1\left(x,y,0\right)=0.02;\quad M_2\left(x,y,0\right)=0.02;\quad \widehat{M}_1\left(x,y,0\right)=0;$$

$$\widehat{M}_2\left(x,y,0\right)=0, N_d\left(x,y,0\right)=0;\quad H\left(x,y,0\right)=\frac{1.3}{10^{11}};\quad T_\beta\left(x,y,0\right)=\frac{1}{10^6};\quad T_\alpha\left(x,y,0\right)=\frac{2}{10^5};$$

$$I_{10}\left(x,y,0\right)=\frac{1}{10^5};\quad P\left(x,y,0\right)=\frac{5}{10^9};\quad A_O\left(x,y,0\right)=0.$$

The parameters and their values are given by the following:

$$D_{A_O}=\left(4.32\times10^{-2}\right)^q;\quad D_H=\left(8.11\times10^{-2}\right)^q;\quad D_{T_\alpha}=\left(6.55\times10^{-2}\right)^q;\quad D_{T_\beta}=\left(6.55\times10^{-2}\right)^q;\quad D_{I_{10}}=\left(6.04\times10^{-2}\right)^q;$$

$$D_P=\left(1.2\times10^{-10}\right)^q;\quad \lambda_\beta^i=\left(9.51\times10^{-6}\right)^q;\quad \lambda_N=\left(8\times10^{-9}\right)^q;\quad \lambda_A=8\times10^{-9};\quad \lambda_{\tau_O}=\left(8.1\times10^{-11}\right)^q;$$

$$\lambda_\tau=\left(1.35\times10^{-11}\right)^q;\quad \lambda_F=\left(1.662\times10^{-3}\right)^q;\quad \lambda_{AT_\alpha}=(81.54)^q;\quad \lambda_{AA_\beta^O}=(1.793)^q;\quad \lambda_{A_O}=\left(5\times10^{-2}\right)^q;$$

$$\lambda_H=\left(3\times10^{-5}\right)^q;\quad \lambda_{MF}=\left(2\times10^{-2}\right)^q;\quad \lambda_{MA}=\left(2.3\times10^{-3}\right)^q;\quad \lambda_{M_1T_\beta}=\left(6\times10^{-3}\right)^q;\quad \lambda_{\widehat{M}_1T_\beta}=\left(6\times10^{-4}\right)^q;$$

$$\lambda_{T_\beta M}=\left(1.5\times10^{-2}\right)^q;\quad \lambda_{T_\beta\widehat{M}}=\left(1.5\times10^{-2}\right)^q;\quad \lambda_{T_\beta M_1}=\left(3\times10^{-2}\right)^q;\quad \lambda_{T_\beta\widehat{M}_1}=\left(3\times10^{-2}\right)^q;$$

$$\lambda_{I_{10}M_2}=\left(6.67\times10^{-3}\right)^q;\quad \lambda_{I_{10}\widehat{M}_2}=\left(6.67\times10^{-3}\right)^q;\quad \lambda_{PA}=\left(6.6\times10^{-8}\right)^q;\quad \lambda_{PM_2}=\left(1.32\times10^{-7}\right)^q;\quad \theta=(0.9)^q;$$

$$\alpha=(5)^q;\quad \beta=(10)^q;\quad \gamma=1;\quad d_{A_\beta^i}=(9.51)^q;\quad d_{A_\beta^O}=(9.51)^q;\quad d_{A_\beta^iM}=\left(2\times10^{-3}\right)^q;\quad d_{A_\beta^i\widehat{M}}=\left(10^{-2}\right)^q;\quad d_\tau=(0.77)^q;$$

$$d_{F_i}=\left(2.77\times10^{-3}\right)^q;\quad d_{F_O}=\left(2.77\times10^{-4}\right)^q;\quad d_N=\left(1.9\times10^{-4}\right)^q;\quad d_{NF}=\left(3.4\times10^{-4}\right)^q;$$

$$d_{NT}=\left(1.7\times10^{-4}\right)^q;\quad d_{N_d}M=(0.06)^q;\quad d_{N_d}\widehat{M}=\left(0.06\right);\quad d_AM=\left(1.2\times10^{-3}\right)^q;\quad d_{M_1}=(0.015)^q;$$

$$d_{M_2}=(0.015)^q;\quad d_{\widehat{M}_1}=(0.015)^q;\quad d_{\widehat{M}_2}=(0.015)^q;\quad d_{A_O}=(0.915)^q;\quad d_H=(58.71)^q;\quad d_{T_\alpha}=(55.45)^q;$$

$$d_{T_\beta}=\left(3.33\times10^2\right)^q;\quad d_{I_{10}}=(16.64)^q;\quad d_P=(1.73)^q;\quad R_0=6^q;\quad M_0=\left(5\times10^{-2}\right)^q;\quad N_0=(0.14)^q;\quad M_G^0=(0.047)^q;$$

$$A_0=(0.14)^q;\quad \overline{K}_{A_\beta^O}=\left(7\times10^{-3}\right)^q;\quad \overline{K}_{N_d}=(10-3)^q;\quad K_{I_{10}}=\left(2.5\times10^{-6}\right)^q;\quad K_{T_\beta}=\left(2.5\times10^{-7}\right)^q;\quad K_M=(0.047)^q;$$

$$K_{\widehat{M}}=(0.047)^q;\quad K_{M_1}=(0.03)^q;\quad K_{M_1}=(0.017)^q;\quad K_{\widehat{M}_1}=\left(\left(0.04\right)\right)^q;\quad K_{\widehat{M}_2}=(0.007)^q;$$

$$K_{F_i}=\left(3.36\times10^{-10}\right)^q;\quad K_{F_O}=\left(2.58\times10^{-11}\right)^q;\quad K_{A_O}=\left(1\times10^{-7}\right)^q;\quad K_P=\left(6\times10^{-9}\right)^q;\quad K_{T_\alpha}=\left(4\times10^{-5}\right)^q;$$

Now by applying the Caputo fractional derivative for each variable of the AD system we get:

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{\left(A_\beta^i\right)'}{(t-x)^q}dx = \left(\lambda_\beta^i\left(1+R\right) - d_{A_\beta^i}A_\beta^i\right)N\Big/N_0$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{\left(A_\beta^0\right)'}{(t-x)^q}dx = A_\beta^i\left|\frac{\partial N}{\partial t}\right| + \frac{\lambda_N N}{N_0} + \frac{\lambda_A A}{A_0} - \left(d_{A_\beta^0\widehat{M}}\left(\widehat{M}_1+\widehat{M}_2\theta\right) + d_{A_\beta^0 M}(M_1+M_2\theta)\right)\frac{A_\beta^0}{A_\beta^0+\overline{K}_{A_\beta^0}}$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{\tau'}{(t-x)^q}dx = \frac{N}{N_0}\left(\lambda_{\tau_0} + \lambda_\tau R - d_\tau \tau\right)$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(F_i)'}{(t-x)^q}dx = \frac{N}{N_0}\left(\lambda_F \tau - d_{F_i}F_i\right)$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(F_o)'}{(t-x)^q}dx = F_i\left|\frac{\partial N}{\partial t}\right| - f_{F_o}F_o$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{N'}{(t-x)^q}dx = \frac{-d_{NF}F_iN}{F_i+K_{F_i}} - \frac{d_{NT}T_\alpha N}{\left(T_\alpha+K_{T_\alpha}\right)\left(K_{I_{10}}+\gamma I_{10}\right)}\Bigg)$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{A'}{(t-x)^q}dx = \lambda_{AA_\beta^o}A_\beta^o + \lambda_{AT_\alpha}T_\alpha - d_A A,$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(N_d)'}{(t-x)^q}dx = \frac{d_{NF}F_iN}{F_i+K_{F_i}} + \frac{d_{NT}T_\alpha N K_{I_10}}{\left(T_\alpha+K_{T_\alpha}\right)\left(K_{I_{10}}+\gamma I_{10}\right)} - d_{N_dM}(M_1+M_2)\frac{N_d}{N_d+\overline{K}_{N_d}} -$$

$$d_{N_d\widehat{M}}\left(\widehat{M}_1+\widehat{M}_2\right)\frac{N_d}{N_d+\overline{K}_{N_d}}$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(A_O)'}{(t-x)^q}dx = \lambda_{A_O}A_\beta^o - d_{A_O}A_O + D_{A_O}\Delta A_O$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{H'}{(t-x)^q}dx = \lambda_H N_d - d_H H + D_H\Delta H$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(M_1)'}{(t-x)^q}dx = \left(\frac{M_G^0\lambda_{MF}F_o}{F_o+K_{F_o}} + \frac{M_G^0\lambda_{MA}A_O}{A_O+K_{A_O}}\right)\frac{\beta\epsilon_1}{\beta\epsilon_1+\epsilon_2} - \nabla\cdot\left(M_1\nabla H\right) + \frac{T_\beta M_1\lambda_{M_1T_\beta}}{T_\beta+K_{T_\beta}} - d_{M_1}M_1$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(M_2)'}{(t-x)^q}dx = \left(\frac{M_G^0\lambda_{MF}F_o}{F_o+K_{F_o}} + \frac{M_G^0\lambda_{MA}A_O}{A_O+K_{A_O}}\right)\frac{\epsilon_2}{\beta\epsilon_1+\epsilon_2} - \nabla\cdot\left(M_2\nabla H\right) + \frac{T_\beta M_2\lambda_{M_2T_\beta}}{T_\beta+K_{T_\beta}} - d_{M_2}M_2$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{\left(\widehat{M}_1\right)'}{(t-x)^q}dx = \alpha\left(P\right)\left(M_0-\widehat{M}\right)\frac{\beta\epsilon_1}{\beta\epsilon_1+\epsilon_2} - \nabla\cdot\left(\widehat{M}_1\nabla A_O\right) + \frac{T_\beta\widehat{M}_1\lambda_{\widehat{M}_1T_\beta}}{T_\beta+K_{T_\beta}} - d_{\widehat{M}_1}\widehat{M}_1$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{\left(\widehat{M}_2\right)'}{(t-x)^q}dx = \alpha\left(P\right)\left(M_0-\widehat{M}\right)\frac{\epsilon_2}{\beta\epsilon_1+\epsilon_2} - \nabla\cdot\left(\widehat{M}_2\nabla A_O\right)$$

$$+\frac{T_\beta\widehat{M}_2\lambda_{\widehat{M}_2T_\beta}}{T_\beta+K_{T_\beta}} - d_{\widehat{M}_2}\widehat{M}_2$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(T_\beta)'}{(t-x)^q}dx = \lambda_{T_\beta M}M_2 + D_{T_\beta}\Delta T_\beta + \lambda_{T_\beta\widehat{M}}\widehat{M}_2 - d_{T_\beta}T_\beta$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(I_{10})'}{(t-x)^q}dx = \lambda_{I_{10}M}M_2 + D_{I_{10}}\Delta T_\beta + \lambda_{I_{10}\widehat{M}}\widehat{M}_2 - d_{I_{10}}I_{10}$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{(T_\alpha)'}{(t-x)^q}dx = \lambda_{T_\alpha M_1}M_1 + D_{T_\alpha}\Delta T_\alpha + \lambda_{T_\alpha\widehat{M}_1}\widehat{M}_1 - d_{T_\alpha}T_\alpha$$

$$\frac{1}{\Gamma(1-q)}\int_0^t \frac{P'}{(t-x)^q}dx = \lambda_{PA}A + D_P\Delta P_{\lambda_{PM_2}M_2} - d_P P.$$

Each variable in the AD system will be expanded with respect to t by using the truncated representation $\mathscr{S}_n$ that extracted from Eq. 2.1, where

$$\mathscr{S}_n g = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbb{Z}}\left\langle g, \psi_{j,k}^\ell\right\rangle\psi_{j,k}^\ell = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbb{Z}}c_g\psi_{j,k}^\ell.$$

Thus,

$$A_{\beta'}^i \approx \mathscr{S}_{nA_\beta^i} = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{A_\beta^i}\psi_{j,k}^\ell\left(t\right);\ A_{\beta'}^0 \approx \mathscr{S}_n A_\beta^0 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{A_\beta^0}\psi_{j,k}^\ell\left(t\right),$$

$$\tau' \approx \mathscr{S}_n\tau = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_\tau\psi_{j,k}^\ell\left(t\right);\ F_i' \approx \mathscr{S}_n F_i' = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{F_i'}\psi_{j,k}^\ell\left(t\right),$$

$$F_o' \approx \mathscr{S}_n F_o' = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{F_o'}\psi_{j,k}^\ell\left(t\right);\ N' \approx \mathscr{S}_n N = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_N\psi_{j,k}^\ell\left(t\right),$$

$$A' \approx \mathscr{S}_n A = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_A\psi_{j,k}^\ell\left(t\right);\ N_d' \approx \mathscr{S}_n N_d = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{N_d}\psi_{j,k}^\ell\left(t\right),$$

$$A_O' \approx \mathscr{S}_n A_O = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{A_O}\psi_{j,k}^\ell\left(t\right);\ H' \approx \mathscr{S}_n H = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_H\psi_{j,k}^\ell\left(t\right),$$

$$N_d' \approx \mathscr{S}_n N_d = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{N_d}\psi_{j,k}^\ell\left(t\right);\ A_O' \approx \mathscr{S}_n A_O = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{A_O}\psi_{j,k}^\ell\left(t\right),$$

$$H' \approx \mathscr{S}_n H = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_H\psi_{j,k}^\ell\left(t\right);\ M_1' \approx \mathscr{S}_n M_1 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{M_1}\psi_{j,k}^\ell\left(t\right),$$

$$M_1' \approx \mathscr{S}_n M_1 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{M_1}\psi_{j,k}^\ell\left(t\right);\ M_2' \approx \mathscr{S}_n M_2 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{M_2}\psi_{j,k}^\ell\left(t\right);$$

$$\widehat{M}_1' \approx \mathscr{S}_n\widehat{M}_1 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{\widehat{M}_1}\psi_{j,k}^\ell\left(t\right);\ \widehat{M}_2' \approx \mathscr{S}_n\widehat{M}_2 = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}}c_{\widehat{M}_2}\psi_{j,k}^\ell\left(t\right),$$

$$T_\beta{}' \approx \mathscr{S}_n T_\beta = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}} c_{T_\beta}\psi_{j,k}^{\ell}\left(t\right); I'_{10} \approx \mathscr{S}_n I_{10} = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}} c_{I_{10}}\psi_{j,k}^{\ell}\left(t\right),$$

$$P' \approx \mathscr{S}_n P = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}} c_{P}\psi_{j,k}^{\ell}\left(t\right); T'_\alpha \approx \mathscr{S}_n T_\alpha = \sum_{\ell=1}^{r}\sum_{j<n}\sum_{k\in\mathbf{Z}} c_{T_\alpha}\psi_{j,k}^{\ell}\left(t\right).$$

Applying the method proposed in [44] reveals us with the following reduced system

$$A_\beta^i\left(t,x,y\right) - A_\beta^i\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_1\left(s,A_\beta^i(s,x,y)\right)}{(t-s)^{1-q}}ds = 0;$$

$$A_\beta^0\left(t,x,y\right) - A_\beta^0\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_2\left(s,A_\beta^0(s,x,y)\right)}{(t-s)^{1-q}}ds = 0;$$

$$\tau\left(t,x,y\right) - \tau\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_3(s,\tau(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$F_i\left(t,x,y\right) - F_i\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_4(s,F_i(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$F_o\left(t,x,y\right) - F_o\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_5(s,F_o(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$N\left(t,x,y\right) - N\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_6(s,N(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$A\left(t,x,y\right) - A\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_7(s,A(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$N_d\left(t,x,y\right) - N_d\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_8(s,N_d(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$A_O\left(t,x,y\right) - A_O\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_9(s,A_O(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$H\left(t,x,y\right) - H\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{10}(s,H(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$M_1\left(t,x,y\right) - M_1\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{11}(s,M_1(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$M_2\left(t,x,y\right) - M_2\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{12}(s,M_2(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$\widehat{M}_1\left(t,x,y\right) - \widehat{M}_1\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{13}\left(s,\widehat{M}_1\left(s,x,y\right)\right)}{(t-s)^{1-q}}ds = 0;$$

$$\widehat{M}_2\left(t,x,y\right) - \widehat{M}_2\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{14}\left(s,\widehat{M}_2\left(s,x,y\right)\right)}{(t-s)^{1-q}}ds = 0;$$

$$T_\beta\left(t,x,y\right) - T_\beta\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{15}(s,T_\beta(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$I_{10}\left(t,x,y\right) - I_{10}\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{16}(s,I_{10}(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$T_\alpha\left(t,x,y\right) - T_\alpha\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{17}(s,T_\alpha(s,x,y))}{(t-s)^{1-q}}ds = 0;$$

$$P\left(t,x,y\right) - P\left(0,x,y\right) - \frac{1}{\Gamma(q)}\int_0^t \frac{\mathscr{X}_{18}(s,P(s,x,y))}{(t-s)^{1-q}}ds = 0.$$

Using collocation technique, we discretize the domain (for t,x, and y) in h step size in order to obtain a sequence of mesh points as follows: for a framelet partial sum of size J, we set

$$M = 2^J,\quad h = 1/2M,\quad x_0 = 0,\qquad x_{m+1} = x_m + mh,\qquad m = 0,1,\ldots,2M,$$

where the simulation is concluded within the following domain:

$$\Xi = \left\{(x,y) \in \mathbb{R}^2 : 0\leqslant x,\qquad y\leqslant 1\right\}.$$

Therefore,

$$A_\beta^i\left(t_m,x_i,y_j\right) - A_\beta^i\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_1\left(s,A_\beta^i\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$A_\beta^0\left(t_m,x_i,y_j\right) - A_\beta^0\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_2\left(s,A_\beta^0\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$\tau\left(t_m,x_i,y_j\right) - \tau\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_3\left(s,\tau\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$F_i\left(t_m,x_i,y_j\right) - F_i\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_4\left(s,F_i\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$F_o\left(t_m,x_i,y_j\right) - F_o\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_5\left(s,F_o\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$N\left(t_m,x_i,y_j\right) - N\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_6\left(s,N\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$A\left(t_m,x_i,y_j\right) - A\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_7\left(s,A\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$N_d\left(t_m,x_i,y_j\right) - N_d\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_8\left(s,N_d\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$A_O\left(t_m,x_i,y_j\right) - A_O\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_9\left(s,A_O\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$H\left(t_m,x_i,y_j\right) - H\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t} \frac{\mathscr{X}_{10}\left(s,H\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$M_1\left(t_m,x_i,y_j\right) - M_1\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{11}\left(s,M_1\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$M_2\left(t_m,x_i,y_j\right) - M_2\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{12}\left(s,M_2\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$\widehat{M}_1\left(t_m,x_i,y_j\right) - \widehat{M}_1\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{13}\left(s,\widehat{M}_1\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$\widehat{M}_2\left(t_m,x_i,y_j\right) - \widehat{M}_2\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{14}\left(s,\widehat{M}_2\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$T_\beta\left(t_m,x_i,y_j\right) - T_\beta\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{15}\left(s,T_\beta\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$I_{10}\left(t_m,x_i,y_j\right) - I_{10}\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{16}\left(s,I_{10}\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$T_\alpha\left(t_m,x_i,y_j\right) - T_\alpha\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{17}\left(s,T_\alpha\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0;$$

$$P\left(t_m,x_i,y_j\right) - P\left(0,x_i,y_j\right) - \frac{1}{\Gamma(q)}\int_0^{t_m} \frac{\mathscr{X}_{18}\left(s,P\left(s,x_i,y_j\right)\right)}{(t_m-s)^{1-q}}ds = 0.$$

$$\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_1\left(s_n,A_\beta^i\left(s_n,x_i,y_j\right)\right)}{(t_m-s_n)^{1-q}} - \frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_1\left(s_{n+1},A_\beta^i\left(s_{n+1},x_i,y_j\right)\right)}{(t_m-s_{n+1})^{1-q}}.$$

Now, by approximating the integrals in the proposed model based on the composite trapezoidal rule, we have,

$$A_{\beta}^{i}\left(t_m,x_i,y_j\right)=A_{\beta}^{i}\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_1\left(s_n,A_{\beta}^{i}\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_1\left(s_{n+1},A_{\beta}^{i}\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$A_{\beta}^{0}\left(t_m,x_i,y_j\right)=A_{\beta}^{0}\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_2\left(s_n,A_{\beta}^{0}\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_2\left(s_{n+1},A_{\beta}^{0}\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$\tau\left(t_m,x_i,y_j\right)=\tau\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_3\left(s_n,\tau\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_3\left(s_{n+1},\tau\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$F_i\left(t_m,x_i,y_j\right)=F_i\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_4\left(s_n,F_i\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_4\left(s_{n+1},F_i\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$F_o\left(t_m,x_i,y_j\right)=F_o\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_5\left(s_n,F_o\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_5\left(s_{n+1},F_o\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$N\left(t_m,x_i,y_j\right)=N\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_6\left(s_n,N\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_6\left(s_{n+1},N\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$A\left(t_m,x_i,y_j\right)=A\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_7\left(s_n,A\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_7\left(s_{n+1},A\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$N_d\left(t_m,x_i,y_j\right)=N_d\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_8\left(s_n,N_d\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_8\left(s_{n+1},N_d\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$A_O\left(t_m,x_i,y_j\right)=A_O\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_9\left(s_n,A_O\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_9\left(s_{n+1},A_O\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$H\left(t_m,x_i,y_j\right)=H\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{10}\left(s_n,H\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{10}\left(s_{n+1},H\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$M_1\left(t_m,x_i,y_j\right)=M_1\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{11}\left(s_n,M_1\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{11}\left(s_{n+1},M_1\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$M_2\left(t_m,x_i,y_j\right)=M_2\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{12}\left(s_n,M_2\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{12}\left(s_{n+1},M_2\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$\widehat{M}_1\left(t_m,x_i,y_j\right)=\widehat{M}_1\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{13}\left(s_n,\widehat{M}_1\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{13}\left(s_{n+1},\widehat{M}_1\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$\widehat{M}_2\left(t_m,x_i,y_j\right)=\widehat{M}_2\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{14}\left(s_n,\widehat{M}_2\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{14}\left(s_{n+1},\widehat{M}_2\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$T_{\beta}\left(t_m,x_i,y_j\right)=T_{\beta}\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{15}\left(s_n,T_{\beta}\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{15}\left(s_{n+1},T_{\beta}\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$I_{10}\left(t_m,x_i,y_j\right)=I_{10}\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{16}\left(s_n,I_{10}\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{16}\left(s_{n+1},I_{10}\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$T_{\alpha}\left(t_m,x_i,y_j\right)=T_{\alpha}\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{17}\left(s_n,T_{\alpha}\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{17}\left(s_{n+1},T_{\alpha}\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}};$$

$$P\left(t_m,x_i,y_j\right)=P\left(0,x_i,y_j\right)+\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{18}\left(s_n,P\left(s_n,x_i,y_j\right)\right)}{\left(t_m-s_n\right)^{1-q}}-\frac{1}{\Gamma(q)}\sum_{n=0}^{2m-1}\frac{\mathscr{X}_{18}\left(s_{n+1},P\left(s_{n+1},x_i,y_j\right)\right)}{\left(t_m-s_{n+1}\right)^{1-q}}.$$

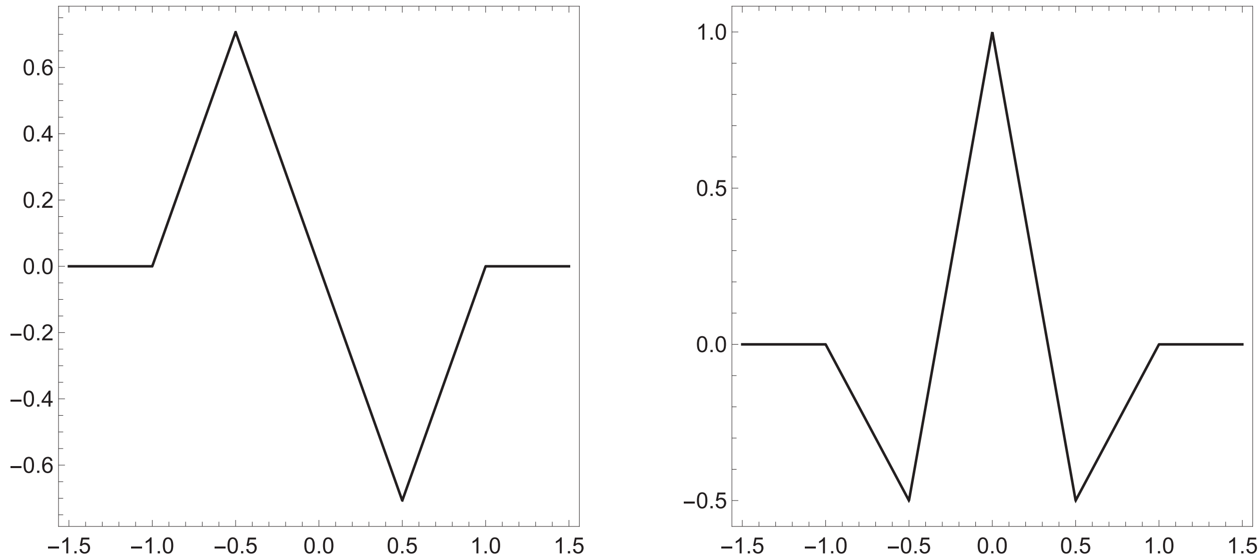


Fig. 1. The graphs of generators ψ_1, ψ_2 in Example 0.1.

Thus, the AD system will be reduced to a matrix system that numerically can be easily solved to get the approximate solution for each variable (see Figs. 1 and 2).

By joining the variables and solving the resulting system, we present the simulation results of the PDE system of AD fractional model in Figs. 3–7. The plots represent the average density for all variables of the new model considering different values of fractional orders, namely $q = 0.7, q = 0.8$ and $q = 1$. In Fig. 8 we show the number of neurons for $q = 1, 0.8, 0.7$ depending on A_β^0, T_β and P.

Conclusion

In this paper, we investigated and constructed a new mathematical model of AD, that is initially formulated based on the classical ordinary integer derivative, by extending the base model to a fractional system of PDEs and by involving the Caputo fractional derivative. There are many advantages of using such derivative which resulted in better describing the dynamics of such disease. Thus, the fractional-order model provides better results than the integer-order model.

The new system is simulated by means of framelet approximation/expansion where an explicit form of the framelets (generators) of such method is given explicitly. The generators through out the work is constructed using important set of non-negative functions, namely the B-splines, and based on the unitary and oblique extension principles. Using such approach is to provide us with an approximated simulation of the new mathematical AD model with high accuracy order, compactly supported framelets, high vanishing moments, and a proper properties of smoothness and symmetries.

We provided several graphical illustrations for all of the simulated variables to visualize their behavior for interpretation. For example, in Figs. 3,4,6,7 the results represent the average density for all variables of the new model using different values of fractional orders. It confirm that the variables just keep a consistent pace and so a steady state behavior with different values of fractional order. In Fig. 8, the results show that neurons are increasingly dying according to the fractional order values.

The obtained results provide us with a fundamental information to further better recognize the dynamics of AD. This may give some insights to researchers in future practical medical trails for many applications.

Compliance with ethics requirements

This article does not contain any studies with human or animal subjects.

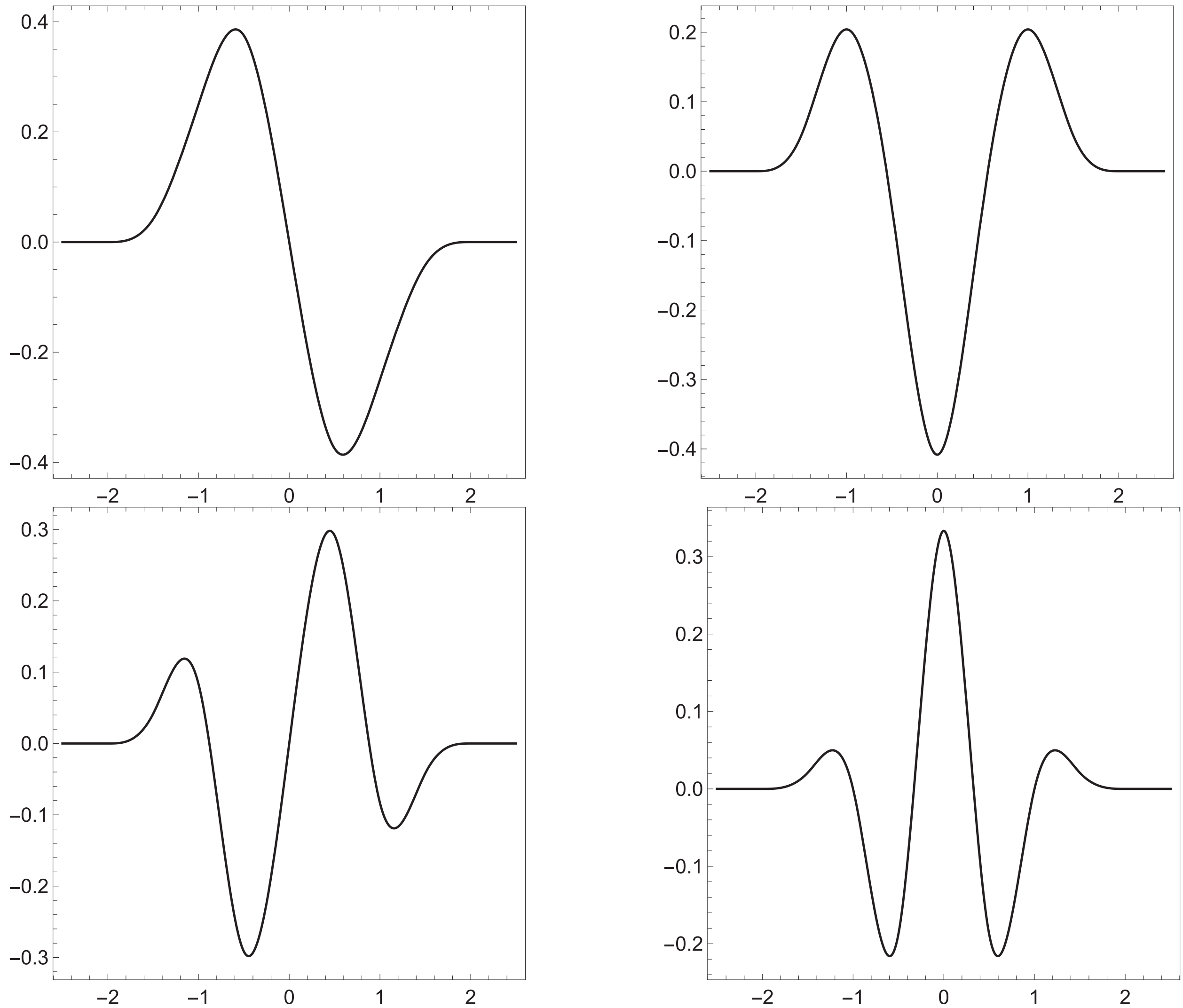
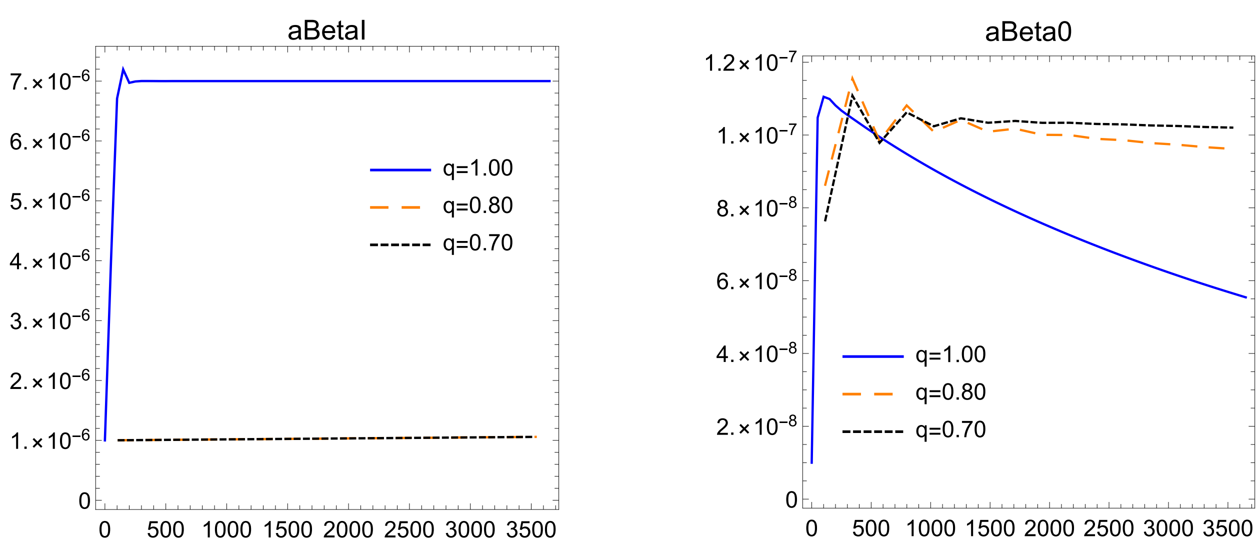
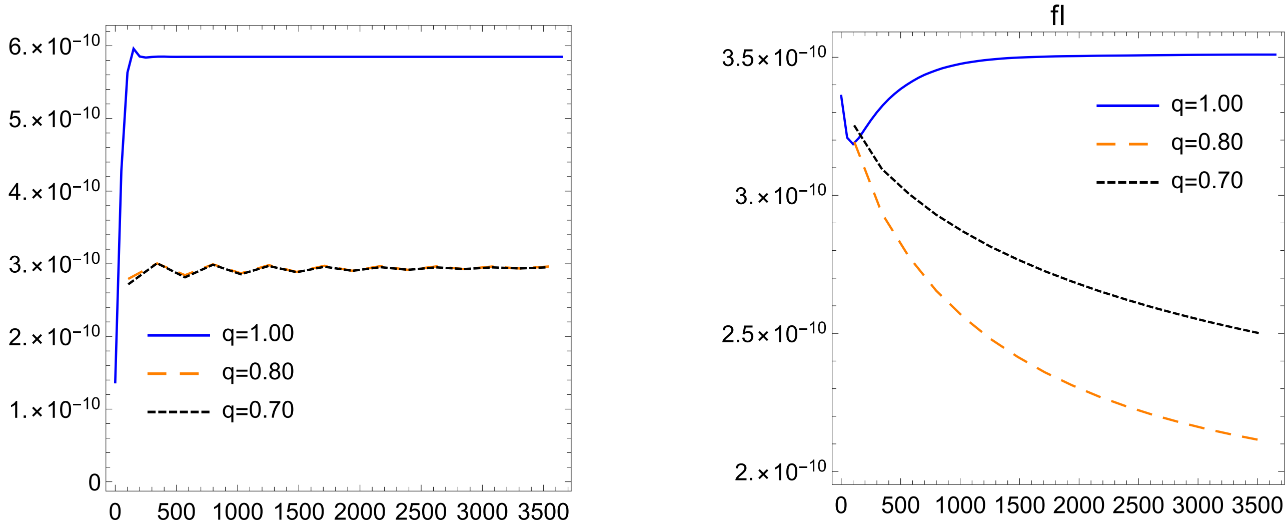


Fig. 2. The graphs of generators $\psi_1, \ldots, \psi_4$ in Example 0.2.



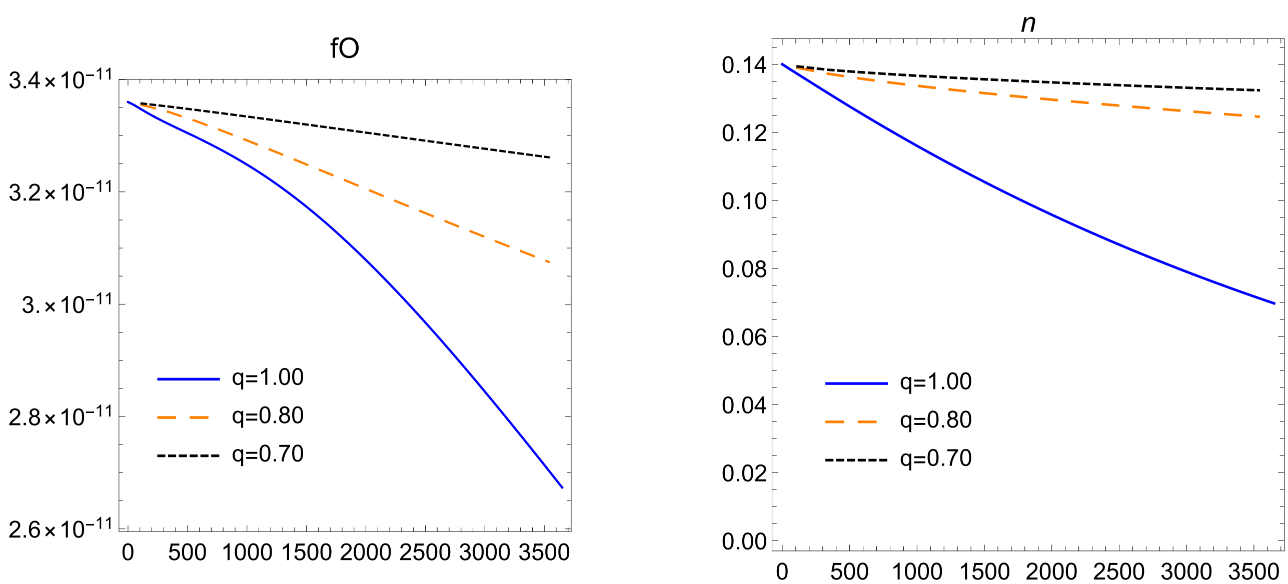
(a) A^i_β **(b)** A^0_β

Fig. 3. The average density of some variables as indicated under each subfigure for different values of q.



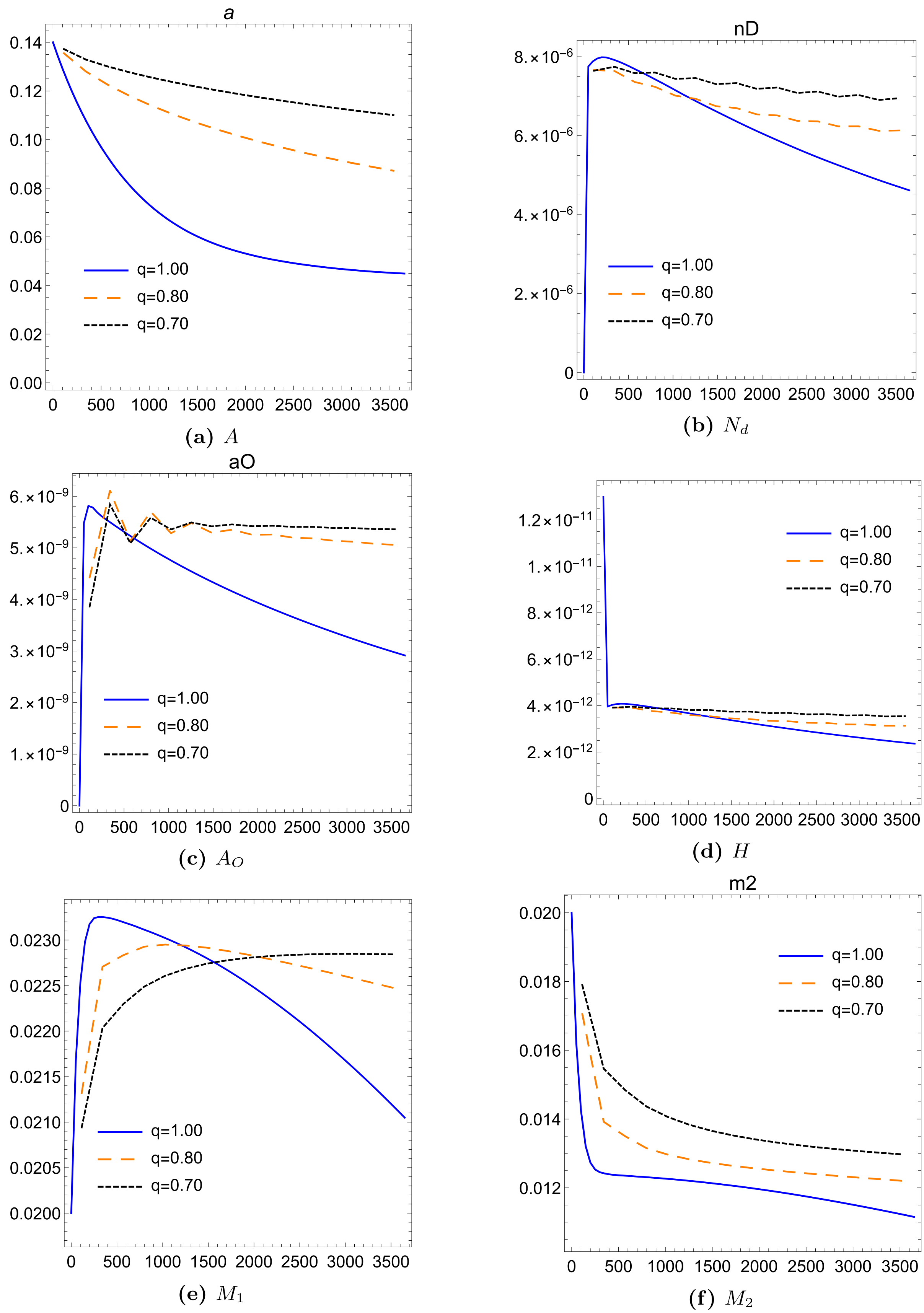
(a) τ **(b)** F_i

Fig. 4. The average density of some variables as indicated under each subfigure for different values of q.



(a) F_o **(b)** N

Fig. 5. The average density of some variables as indicated under each subfigure for different values of q.

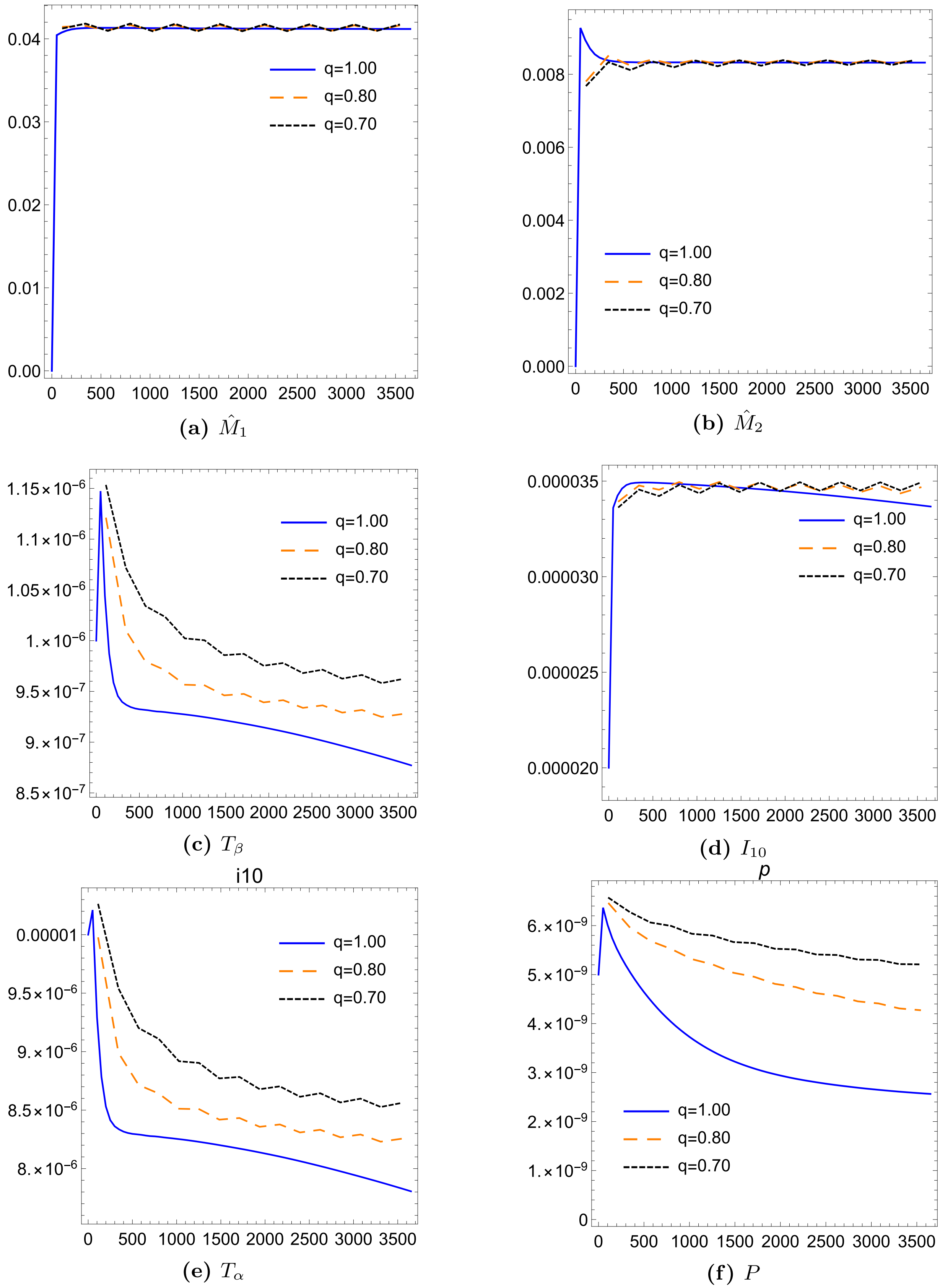


(a) A **(b)** N_d

(c) A_O **(d)** H

(e) M_1 **(f)** M_2

Fig. 6. The average density of some variables as indicated under each subfigure for different values of q.

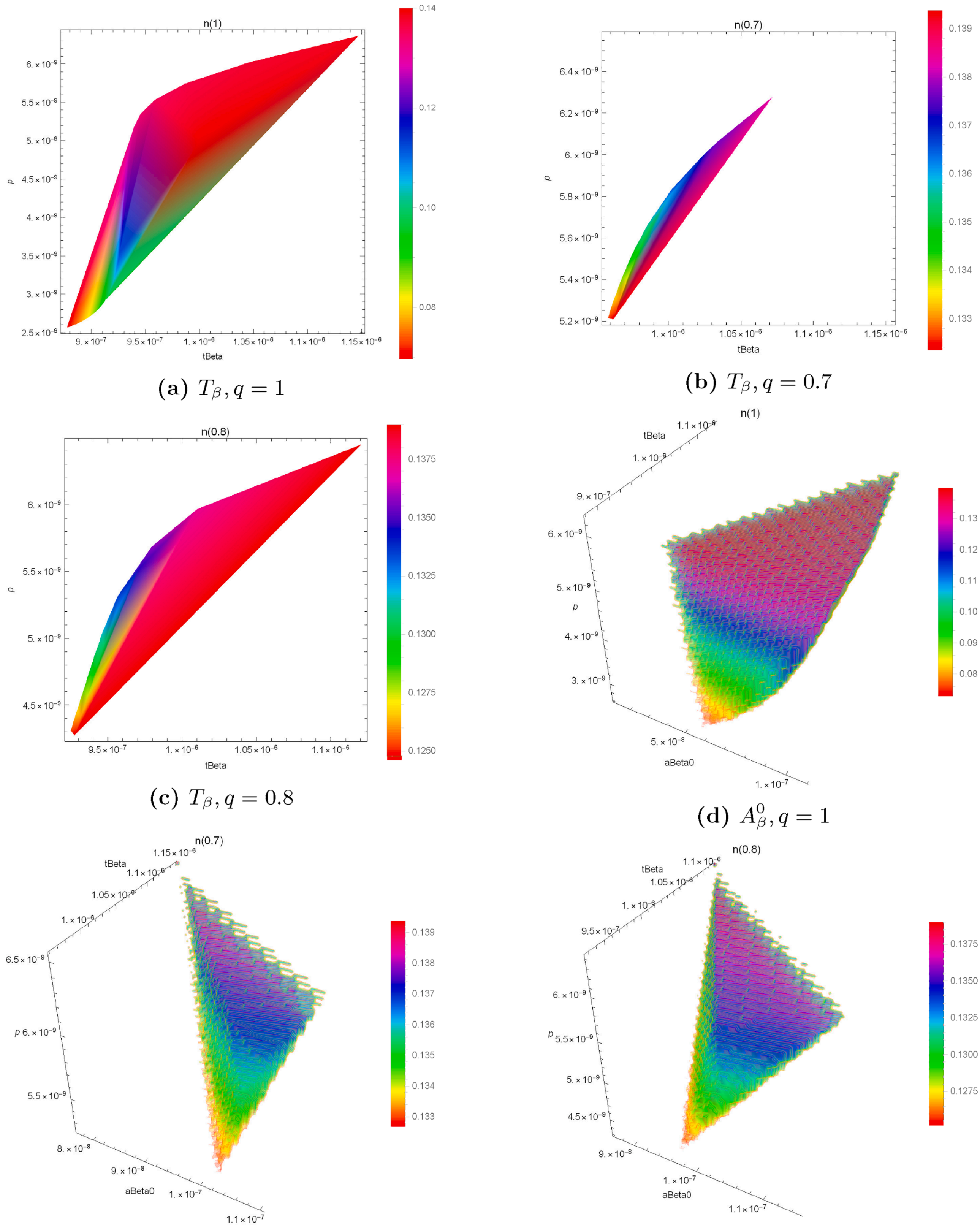


(a) $\hat{M}_1$ (b) $\hat{M}_2$

(c) T_β (d) I_{10}

(e) T_α (f) P

Fig. 7. The average density of some variables as indicated under each subfigure for different values of *q*.



(a) $T_\beta, q = 1$

(b) $T_\beta, q = 0.7$

(c) $T_\beta, q = 0.8$

(d) $A^0_\beta, q = 1$

(e) $A^0_\beta, q = 0.7$

(f) $A^0_\beta, q = 0.8$

Fig. 8. The number of neurons when $q = 1, 0.8, 0.7$ depending on A^0_β, T_β and P.

CRediT authorship contribution statement

Mutaz Mohammad: Conceptualization, Methodology, Software, Investigation, Supervision, Validation, Writing - review & editing. **Alexander Trounev:** Software.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Further reading

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