Multi-term fractional equations modeling oxygen delivery through capillaries to tissues

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Outline

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General form of fractional derivatives

Let

- $\mathcal{N}(t)$ be a given nonnegative locally integrable kernel
- a, b be given quantities (including $\pm\infty$)

The left fractional derivatives ($t > a$):

$$\mathcal{D}^{\mathcal{N}}_{a,t} u(x,t) = \frac{\partial}{\partial t}\int_a^t \mathcal{N}(t-\tau)u(x,\tau)\,d\tau$$
$$-\mathcal{N}(t-a)\cdot\begin{cases} u(x,a) & \text{in more regular case,} \\ 0 & \text{otherwise,}\end{cases}$$

or (in more regular case)

$$\mathcal{D}^{\mathcal{N}}_{a,t} u(x,t) = \int_a^t \mathcal{N}(t-\tau)\frac{\partial u}{\partial t}(x,\tau)\,d\tau.$$

The right fractional derivatives: $t < b$

$$\mathcal{D}_{t,b}^{\mathcal{N}} u(x,t) = -\frac{\partial}{\partial t}\int_t^b \mathcal{N}(\tau - t)\, u(x,\tau)\, d\tau$$

$$- \mathcal{N}(b-t) \cdot \begin{cases} u(x,b) & \text{in more regular case,} \\ 0 & \text{otherwise,} \end{cases}$$

or (in more regular case)

$$\mathcal{D}_{t,b}^{\mathcal{N}} u(x,t) = -\int_t^b \mathcal{N}(\tau - t)\frac{\partial u}{\partial t} u(x,\tau)\, d\tau,$$

- *The (left) Caputo fractional derivative:*

$$\mathcal{N}(t) = \frac{t^{-\nu}}{\Gamma(1-\nu)}, \qquad \nu \in (0,1)$$

with $\Gamma(\cdot)$ being the Euler Gamma function:

$$\mathcal{D}^{\mathcal{N}}_{0,t} u(x,t) = \mathbf{D}^{\nu}_t u(x,t) = \frac{1}{\Gamma(1-\nu)} \frac{\partial}{\partial t} \int\limits_0^t \frac{u(x,s) - u(x,0)}{(t-s)^{\nu}} \, ds,$$

or an equivalent definition

$$\mathcal{D}^{\mathcal{N}}_{0,t} u(x,t) = \mathbf{D}^{\nu}_t u(x,t) = \frac{1}{\Gamma(1-\nu)} \int\limits_0^t (t-s)^{-\nu} \frac{\partial u}{\partial s}(x,s) \, ds,$$

if u is an absolutely continuous function.

- Multi-term fractional derivatives:

$$\mathcal{N}(t) = \sum_{i=0}^{M} q_i \frac{t^{-\nu_i}}{\Gamma(1-\nu_i)},$$

$$1 > \nu_0 > \nu_1 > ... > \nu_M > 0, \quad q_i \geq 0,$$

multi-term Caputo fractional derivative (left):

$$\mathcal{D}_{0,t}^{\mathcal{N}} u(x,t) = \sum_{i=0}^{M} q_i \mathbf{D}_t^{\nu_i} u(x,t),$$

multi-term R-L fractional derivative (left):

$$\mathcal{D}_{0,t}^{\mathcal{N}} u(x,t) = \sum_{i=0}^{M} q_i \partial_t^{\nu_i} u(x,t),$$

In general, q_i remaining nonnegative may depend on some parameters, e.g. x.

Anomalous diffusion equations: "Macro level" approach

Conservative laws+ specific relations with memory (*Caputo*&Plastino 2000-2011, Srivastava&Rai 2010, Hu, Zhang&Li 2022)
Let

- u be the fluid mass per unit volume;
- v be the flux rate;
- p be the pressure of the fluid

Constitutive relations including memory: $A_i, B_i \geq 0, \mathcal{N}_i \geq 0$,

$$\begin{cases} A_1 v + \mathcal{D}_{0,t}^{\mathcal{N}_1} v = -B_1 \nabla p - \mathcal{D}_{0,t}^{\mathcal{N}_2} \nabla p, \\ A_2 u + \mathcal{D}_{0,t}^{\mathcal{N}_3} u = B_2 p + \mathcal{D}_{0,t}^{\mathcal{N}_4} \nabla p, \end{cases}$$

Conservative law:

$$\text{div}\, v + \frac{\partial u}{\partial t} = q(u)$$

($q(u)$ is a source term).

Models of flux in porous media with memory (Caputo et al, 2000-2011)

$$\mathcal{N}_i \equiv 0, \quad i = 1, 3, 4, \quad \mathcal{N}_2 = B\frac{t^{-\nu}}{\Gamma(1-\nu)}, \quad \nu \in (0,1),$$
$$A_j, B_j, B > 0,$$

then

$$\begin{cases} A_1 v = -B_1 \nabla p - B\mathbf{D}_t^{\nu} \nabla p, \\ A_2 u = B_2 p, \end{cases}$$

Subdiffusion equation with the memory term:

$$\mathbf{D}_t^{1-\nu} p(x,t) - \frac{B_2 B_1}{A_2 A_1} \mathcal{N}_2 \star \Delta p - \frac{B_2 B}{A_2 A_1} \Delta p(x,t) = q(t, \nu, p).$$

Anomalous diffusion equations: "Micro level" approach

Modeling continuous time random walk (RW) processes (*Meerschaert&Sikorskii, 2003-2012, Metzler, 2014-2018*):

• **Normal Diffusion**:

Classical Random Walk (CRW) + Central Limit Theorem(CLT)

$\Rightarrow$ **Classical ADE** for the density of the distribution

Let

Y_i be independent and identically distribution random variables, that represent the jumps of randomly selected particle.

Main assumptions: (normal distribution)

Finite variance jump length distribution σ,

Finite mean distribution μ.

The random walk: $S_n = \sum_{i=1}^{M} Y_i$, gives the location of the particle after n jumps.

CLT leads

$$\frac{S_n - n\mu}{\sigma\sqrt{n}} \to N(0,1) - \text{normal distribution with mean zero and variance} = 1$$

Putting

$$n = \frac{t}{\delta t}, \quad A = \frac{\mu}{\Delta t}, \quad D = \frac{\sigma^2}{2\Delta t},$$

we conclude that *R*W has Gaussian distribution with the density solving the classical ADE:

$$\frac{\partial C}{\partial t} = -A\frac{\partial C}{\partial x} + D\frac{\partial^2 C}{\partial x^2}.$$

- **Anomalous Diffusion**

Limiting stochastic process ↓ Governing equation ↓ Solution	Finite-variance jump length distribution	Infinite-variance jump length distribution
Finite-mean waiting time distribution	Brownian motion ↓ ADE ↓ Gaussian density	Lévy motion ↓ Fractional-in-space ADE ↓ α-stable density
Infinite-mean waiting time distribution	Brownian motion subordinated to inverse Lévy Process ↓ Fractional-in-time ADE ↓ Subordinated Gaussian density	Lévy motion subordinated to inverse Lévy Process ↓ Fractional-in-space-time ADE ↓ Subordinated α-stable density

Let Y_i have the heavy-tailed distribution with the density $p(x)$, i.e.

$$\sigma^2 = \int_{-\infty}^{+\infty} p(x)(Y_i - \mu)^2\, dx \to +\infty.$$

Example is the Pareto distribution centered to mean zero

$$p(x) = \begin{cases} c\nu x^{\nu-1}, & x \geq c_0^{1/\nu}, \\ 0, & x < c_0^{1/\nu}, then \end{cases}$$

$C(x,t)$, the density of distribution to "anomalous" *RW*, is called ν-stable and solves the equation

$$\frac{\partial C}{\partial t} = -A\frac{\partial C}{\partial x} + D\partial_x^\nu C, \quad \nu \in (1,2).$$

Oxygen diffusion through capillaries

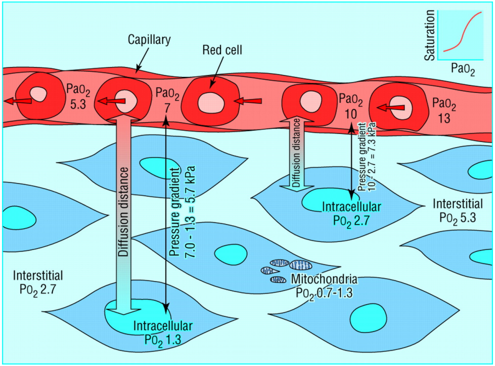

Figure: **Oxygen transport through a single capillary.** *Source: This figure is taken from R.M. Leach, D.F. Treacher, Oxygen transport-2. Tissue hypoxia, Clinical Rev. BMJ, 317(1998)*

Methods to measure the oxygen level

- **in vivo**: two-photon phosphorescence lifetime microscopy (in vivo), (Lecoq, Parpaleix and et al., 2011).

  However, the existence techniques can hardly offer a complete spatial-temporal picture of the oxygen filed on microscopic scales.

- **in vitro**: analytical studying including:

  theoretical modeling (Krogh, 1930, Popel 1982-1989, Wang 2001, Go 2007)

  numerical simulation (Goldman&Popel 2001, Wood & et al. 2009, Secomb & et al. 2004)

Models with the normal diffusion

$$\frac{\partial \mathfrak{C}}{\partial t} - \mathfrak{d}\Delta\mathfrak{C} + k = 0,$$

$\mathfrak{C} = \mathfrak{C}(r, \varphi, x, t)$ is the concentration of oxygen,
k is the consumption constant per volume of tissue,
$\mathfrak{d}$ is the diffusion coefficient of oxygen.

• The (first) classical **Krogh**(1920) cylinder model roughly describes the oxygen transport
(• *passive diffusion driven by gradients of oxygen tension;* • *a simple geometrical model;* • *for a single capillary*);

• **Goldman**&**Poeppel** (2001,2003), **Go** (2007) proposed models to a relatively complex vessel network structure.

• *the longitudinal diffusion of solute was neglected,*

• *the diffusion and the consumption rate of oxygen were assumed to be the same everywhere.*

Subdiffusion models

Srivastava&**Rai** (2010):

$$\mathbf{D}_t^{\nu_1}\mathfrak{C} - \tau\mathbf{D}_t^{\nu_2}\mathfrak{C} = \operatorname{div}(\mathfrak{d}\nabla\mathfrak{C}) - k, \quad 0 < \nu_2 < \nu_1 \leq 1.$$

$\mathfrak{d} = \mathfrak{d}(r, \varphi, x, t, \mathfrak{C})$,
$\tau = const. > 0$ is the time lag in concentration of oxygen along the capillary,
$\mathbf{D}_t^{\nu_1}\mathfrak{C} - \tau\mathbf{D}_t^{\nu_2}\mathfrak{C}$ details the net diffusion of oxygen to all tissues.
Srivastava, Tripathi&**Beg** (2017), **Marales-Delgado, Agarwal** & **et al.** (2019):
the model with the presence of external forces

$$\mathbf{D}_t^{\nu_1}\mathfrak{C} - \tau\mathbf{D}_t^{\nu_2}\mathfrak{C} = \operatorname{div}(\mathfrak{d}\nabla\mathfrak{C}) - k - \int_0^t \frac{(t-s)^{\nu_1-1}}{\Gamma(\nu_1)}(\mathfrak{d}_0\nabla\mathfrak{C} + \mathfrak{d}_1\mathfrak{C})\,ds,$$

$\mathfrak{d}_i = \mathfrak{d}_i(r, \varphi, x, t, \mathfrak{C})$ are the diffusion coefficients of oxygen.

Multi-term fractional equations with memory terms

Let $\Omega \in \mathbb{R}^n$, $n \geq 1$, have a smooth boundary $\partial\Omega$,

$$\Omega_T = \Omega \times (0, T), \qquad \partial\Omega_T = \partial\Omega \times [0, T].$$

For fixed $\nu_i \in (0, 1)$, we discuss the equation in the unknown function $u = u(x, t)$: $\Omega_T \to \mathbb{R}$,

$$\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\rho_j u) - \mathcal{L}_1 u - \mathcal{K} \star \mathcal{L}_2 u = f(x, t, u), \tag{1}$$

$\rho_j = \rho_j(x, t)$, $\qquad \rho_1 > 0$,
$0 < \nu_N < \nu_{N-1} < \ldots < \nu_1 < 1$,
$\mathcal{K}$ is a summable convolution kernel,

$$\mathcal{L}_1 = \sum_{ij=1}^{n} a_{ij}(x, t) \frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{n} a_i(x, t) \frac{\partial}{\partial x_i} + a_0(x, t),$$

$$\mathcal{L}_2 = \sum_{ij=1}^{n} b_{ij}(x, t) \frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{n} b_i(x, t) \frac{\partial u}{\partial x_i} + b_0(x, t),$$

Previous investigations of the single-term fractional subdiffusion equation:

$$\mathbf{D}_t^{\nu} u - \mathcal{L}_1 u - \mathcal{K} \star \mathcal{L}_2 u = f(x, t, u), \quad \nu \in (0, 1)$$

- Theory of mild solutions and abstract Cauchy problems (Gal, Kempanien, Bazglekova, Vergara, Zacher, Liazama, Ponce, Kochubei Guerekata...)
- Theory existence of weak and strong solutions (Bazglekova, Vergara, Zacher, Yamamoto, Janno,...)
- Classical solvability, and smooth solutiongs (Krasnoschek, Vasylyeva, Pata, Gudideti, Pskhu)
- Maximum principle, Harnak inequalities, asymptotic (Luchko, Ahmad, Gorenflo, Mainardi, Gal, Zaher, Bazhlekova, KPV...)
- Inverse problems(Yamamoto, Kinah, Janno, Rundal, Kian..)

Previous investigations of the multi-term fractional subdiffusion equation:

$$\frac{\partial}{\partial t}(\mathcal{N} \star u) - \mathcal{L}_1 u = f(x, t). \tag{2}$$

with a strictly positive weakly singular kernel $\mathcal{N} = \mathcal{N}(t)$

- The Cauchy problem to (2) on unbounded domains (*Kochubei, 2011*);
- Maximal principle for IBVP to (2) (*Luchko 2016, Luchko, Suzuki, Yamamoto 2022*);

Previous investigations of the multi-term fractional subdiffusion equation:

$$\sum_{j=1}^{N} q_i(x)\mathbf{D}_t^{\nu_j} u - \mathcal{L}_1 u = f(x,t),\, q_i \geq 0, \quad \nu_j \in (0,1). \tag{3}$$

• The boundary behavior of the eigenfunctions of an equations to (3) (*Carbotti, Dipierro, Valdinoci, 2019*);
• Explicit solutions via series for IBVP to (3) where $q_i = const. > 0$ (*Luchko 2011, Daftardar-Gejji&Bhalekar 2009, Yamamoto& et al. 2015*);
• Solvability of IBVP to (3) with $q_i = q_i(x) > 0$ (*Li, Huang, Yamamoto 2020*);
• Numerical solutions (*Srivastava, Rai 2007, Srivastava et al 2010, Marales-Delgauo et al. 2010, Bazhlekova 2013, Sin, 2018, Zhang et al. 2019*);

Main differences and difficulties of $\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\rho_j u) - \mathcal{L}_1 u - \mathcal{K} \star \mathcal{L}_2 u = f(x, t, u)$

- Caputo fractional derivatives of the product of two functions: $\mathbf{D}_t^{\nu_j}(\rho_j u)$, $\rho_j = \rho_j(x, t)$. The well-known Leibniz rule does not work

$$\mathbf{D}_t^{\nu_j}(\rho_j u) = u(x, 0)\mathbf{D}_t^{\nu_j}\rho_j + \rho_j(x, t)\mathbf{D}_t^{\nu_j} u + \frac{\nu_j}{\Gamma(1-\nu_j)} \int_0^t \frac{[\rho_j(x, t) - \rho_j(x, s)][u(x, s) - u(x, 0)]}{(t-s)^{1+\nu_j}} ds.$$

- under certain assumptions on ϱ_i,

$$\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(u\rho_j) = \frac{\partial}{\partial t}\mathcal{N} \star u, \qquad \mathcal{N} < 0, \quad t > T_0.$$

Indeed, Janno&Kinah (2018) proved if $0 < \nu_2 < \nu_1 < 1$,

$$\frac{t^{-\nu_1}}{\Gamma(1-\nu_1)} - \frac{t^{-\nu_2}}{\Gamma(1-\nu_2)} < 0 \qquad \text{whenever} \qquad t > e^{-0.577}, \Rightarrow$$

$$\mathbf{D}_t^{\nu_1}(\varrho_1 u) - \mathbf{D}_t^{\nu_2}(\varrho_2 u) = \frac{\partial}{\partial t}(\mathcal{N} * u)$$

with $\mathcal{N} = \varrho_1 \frac{t^{-\nu_1}}{\Gamma(1-\nu_1)} - \varrho_2 \frac{t^{-\nu_2}}{\Gamma(1-\nu_2)} < 0$, for $t > e^{-0.577}$, $0 < \varrho_1(x) \leq \varrho_2(x)$.

IBVP to $\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\rho_j u) - \mathcal{L}_1 u - \mathcal{K} \star \mathcal{L}_2 u = f(x,t)$

Initial condition:

$$u(x,0) = u_0(x) \quad \text{in} \quad \bar{\Omega}, \tag{4}$$

boundary conditions on $\partial\Omega_T$:

(i) Dirichlet boundary condition (**DBC**)

$$u(x,t) = \psi_1, \tag{5}$$

(ii) Boundary condition of the third kind (**3BC**)

$$\mathcal{M}_1 u + \mathcal{K}_0 * \mathcal{M}_2 u = \psi_2, \tag{6}$$

(iii) Fractional dynamic boundary condition (**FDBC**)

$$\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\rho_j u) - \mathcal{M}_1 u + \mathcal{K}_0 * \mathcal{M}_2 u = \psi_3. \tag{7}$$

$$\mathcal{M}_1 = \sum_{i=1}^{n} c_i(x,t) \frac{\partial}{\partial x_i} + c_0(x,t),$$

$$\mathcal{M}_2 = \sum_{i=1}^{n} d_i(x,t) \frac{\partial}{\partial x_i} + d_0(x,t).$$

Functional spaces

To global classical solvability

Definition 1

A function $v = v(x,t)$ belongs to the class $C^{l+\alpha, \frac{l+\alpha}{2}\nu}(\bar{\Omega}_T)$, for $l = 0, 1, 2$, $\alpha, \nu \in (0,1)$, if the function v together with its corresponding derivatives are continuous and the norms here below are finite:

$$\|v\|_{C^{l+\alpha, \frac{l+\alpha}{2}\nu}(\bar{\Omega}_T)} = \|v\|_{C([0,T], C^{l+\alpha}(\bar{\Omega}))} + \sum_{|j|=0}^{l} \langle D_x^j v \rangle_{t,\Omega_T}^{(\frac{l+\alpha-|j|}{2}\nu)}, \quad l = 0, 1,$$

$$\|v\|_{C^{2+\alpha, \frac{2+\alpha}{2}\nu}(\bar{\Omega}_T)} = \|v\|_{C([0,T], C^{2+\alpha}(\bar{\Omega}))} + \|\mathbf{D}_t^{\nu} v\|_{C^{\alpha, \frac{\alpha}{2}\nu}(\bar{\Omega}_T)} + \sum_{|j|=1}^{2} \langle D_x^j v \rangle_{t,\Omega_T}^{(\frac{2+\alpha-|j|}{2}\nu)}.$$

To the existence of strong solutions

Definition 2

A function v defined in Ω_T belongs to $\mathfrak{H}_p^{s_1,s_2}(\Omega_T)$ with $p > 1$ and $s_1, s_2 \geq 0$, if $v \in W^{s_1,p}((0,T), L_p(\Omega)) \cap L_p((0,T), W^{s_2,p}(\Omega))$, and the norm here below is finite

$$\|v\|_{\mathfrak{H}_p^{s_1,s_2}(\Omega_T)} = \|v\|_{W^{s_1,p}((0,T),L_p(\Omega))} + \|v\|_{L_p((0,T),W^{s_2,p}(\Omega))}.$$

Assumptions

H1. Conditions on the fractional order of the derivatives: We assume that for $j = 2, ..., N$,

$$\nu_1 \in (0, 1] \qquad \text{and} \qquad \nu_j \in \begin{cases} \left(0, \frac{\nu_1(2-\alpha)}{2}\right), & \text{if either } \textbf{DBC} \text{ or } \textbf{3BC} \text{ hold,} \\ \left(0, \frac{\nu_1(1-\alpha)}{2}\right), & \text{if } \textbf{FDBC} \text{ holds.} \end{cases}$$

H2. Ellipticity conditions on the operators: in particular, $\rho_1(x, t) > 0$, in $\bar{\Omega}_T$

H3. Smoothness of the coefficients: typical for $a_{ij},\ a_i,\ a_0,\ b_{ij},\ b_i,\ b_0,\ c_i,\ d_i$

$$\rho_1 \in \begin{cases} C^{\gamma_0}([0, T], C^1(\bar{\Omega})) & \text{in the } \textbf{DBC} \text{ and } \textbf{3BC} \text{ cases,} \\ C^{\gamma_0}([0, T], C^1(\bar{\Omega})) \cap C^{\gamma_3}([0, T], C^2(\partial\Omega)) & \text{in the } \textbf{FDBC} \text{ case,} \end{cases}$$

$$\rho_j \in \begin{cases} C^{\gamma_j}([0, T], C^1(\bar{\Omega})) & \text{in the } \textbf{DBC} \text{ and } \textbf{3BC} \text{ cases,} \\ C^{\gamma_j}([0, T], C^1(\bar{\Omega})) \cap C^{\gamma_j^*}([0, T], C^2(\partial\Omega)) & \text{in the } \textbf{FDBC} \text{ case,} \end{cases}$$

where

$$\gamma_0 > \frac{\nu_1(2+\alpha)}{2},\ \gamma_j > \frac{\nu_j(2+\alpha)}{2},\ \gamma_3 > \frac{\nu_1(3+\alpha)}{2},\ \gamma_j^* > \frac{\nu_j(3+\alpha)}{2}.$$

H4. Conditions on the given functions

$$\mathcal{K}(t), \mathcal{K}_0(t) \in L_1(0,T),$$

$$u_0(x) \in C^{2+\alpha}(\bar{\Omega}), \quad f(x,t) \in C^{\alpha, \frac{\alpha\nu_1}{2}}(\bar{\Omega}_T),$$

$$\psi_1(x,t) \in C^{2+\alpha, \frac{2+\alpha}{2}\nu_1}(\partial\Omega_T), \quad \psi_2(x,t), \psi_3(x,t) \in C^{1+\alpha, \frac{1+\alpha}{2}\nu_1}(\partial\Omega_T).$$

H5. Compatibility conditions The following compatibility conditions hold for every $x \in \partial\Omega$ at the initial time $t = 0$:

$$\psi_1(x,0) = u_0(x), \quad \sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\varrho_j \psi_1)|_{t=0} = \mathcal{L}_1 u_0(x)|_{t=0} + f(x,0),$$

if the **DBC** holds; and

$$\mathcal{M}_1 u_0(x)|_{t=0} = \psi_2(x,0),$$

if the **3BC** takes place; and in the case of **FDBC**

$$\mathcal{L}_1 u_0(x)|_{t=0} + f(x,0) = \psi_2(x,0) + \mathcal{M}_1 u_0(x)|_{t=0}.$$

Global classical solvability of the linear model

Theorem 1

Let $T > 0$ be fixed, $\partial\Omega \in C^{2+\alpha}$, and let assumptions **H1-H5** hold. Then linear equation (1) with the initial condition (4), subject to either boundary condition **DBC**, **3BC** or **FDBC** admits a unique classical solution $u = u(x,t)$ on $\bar{\Omega}_T$, satisfying the regularity $u \in C^{2+\alpha, \frac{2+\alpha}{2}\nu_1}(\bar{\Omega}_T)$.

$$\|u\|_{C^{2+\alpha,\frac{2+\alpha}{2}\nu_1}(\bar{\Omega}_T)} + \sum_{j=2}^{N} \|\mathbf{D}_t^{\nu_j} u\|_{C^{\alpha,\frac{\alpha}{2}\nu_1}(\bar{\Omega}_T)}$$

$$\leq C \begin{cases} \|f\|_{C^{\alpha,\frac{\alpha}{2}\nu_1}(\bar{\Omega}_T)} + \|u_0\|_{C^{2+\alpha}(\bar{\Omega})} + \|\psi_1\|_{C^{2+\alpha,\frac{2+\alpha}{2}\nu_1}(\partial\Omega_T)} & \textbf{DBC} \text{ case,} \\ \|f\|_{C^{\alpha,\frac{\alpha}{2}\nu_1}(\bar{\Omega}_T)} + \|u_0\|_{C^{2+\alpha}(\bar{\Omega})} + \|\psi_2\|_{C^{1+\alpha,\frac{1+\alpha}{2}\nu_1}(\partial\Omega_T)} & \textbf{3BC} \text{ case,} \end{cases}$$

while if the **FDBC** case holds then

$$\|u\|_{C^{2+\alpha,\frac{2+\alpha}{2}\nu_1}(\bar{\Omega}_T)} + \sum_{j=1}^{N} \|\mathbf{D}_t^{\nu_j} u\|_{C^{\alpha,\frac{\alpha}{2}\nu_1}(\bar{\Omega}_T)\cap C^{1+\alpha,\frac{1+\alpha}{2}\nu_1}(\partial\Omega_T)}$$

$$\leq C[\|f\|_{C^{\alpha,\frac{\alpha}{2}\nu_1}(\bar{\Omega}_T)} + \|u_0\|_{C^{2+\alpha}(\bar{\Omega})} + \|\psi_3\|_{C^{1+\alpha,\frac{1+\alpha}{2}\nu_1}(\partial\Omega_T)}].$$

Global strong solvability for the linear model

For simplicity consideration,

$$\mathbf{D}_t^{\nu_1}(\rho_1 u) - \mathbf{D}_t^{\nu_2}(\rho_2 u) - \mathcal{L}_1 u - \int_0^t \mathcal{K}(t-s)\mathcal{L}_2 u(x,s)\,ds = f(x,t),$$

H6. Representation to ρ_j: We require that ρ_2 retains its sing in $\bar{\Omega}_T$,
If $\rho_2(x,t) > 0$ in $\bar{\Omega}_T$, then $\rho_2 \in C^{\gamma_0}([0,T], C^{1+\alpha}(\bar{\Omega}))$ and

$$\rho_1(x,t) = \rho(x,t) + \rho_2(x,t)$$

with $\rho > 0$ having the same regularity as the function ρ_1.
Moreover, we require that for each $(x,t) \in \bar{\Omega}_T$

$$\frac{\partial}{\partial t}\left(\frac{\rho_1}{\rho_2}\right) \geq 0 \quad \text{if} \quad \rho_2 \quad \text{is negative,}$$

$$\frac{\partial}{\partial t}\left(\frac{\rho_1}{\rho}\right) \leq 0 \quad \text{if} \quad \rho_2 \quad \text{is positive.}$$

The key inequalities in fractional calculus leading to integral estimates:

$$
\begin{aligned}
pw^{p-1}(t)\frac{d}{dt}(\mathcal{N}\star w)(t) &\geq \frac{d}{dt}(\mathcal{N}\star w^p)(t) + (p-1)w^p(t)\mathcal{N}(t) \\
&\geq \frac{d}{dt}(\mathcal{N}\star w^p)(t) \qquad (8)
\end{aligned}
$$

for any integer even $p \geq 2$, a positive summable weakly singular kernel $\mathcal{N}$.

In particular, if $w(x,0) = 0$,

$$
\mathcal{N} = \frac{t^{-\nu_1}}{\Gamma(1-\nu_1)},
$$

then

$$
\partial_t^\theta w^p(t) \leq pw^{p-1}(t)\partial_t^\theta w(t).
$$

(I) We proved that the function $\frac{t^{-\nu}}{\Gamma(1-\nu)}$ is monotonic non-decreasing, i.e.

$$\frac{\partial}{\partial \nu} \frac{t^{-\nu}}{\Gamma(1-\nu)} \geq 0$$

for each $\nu \in (0,1)$ and $t \in [0, T_\nu]$,
where

$$T_\nu = e^{-\gamma - S(\nu)},$$

with γ being the Euler-Mascheroni constant, and

$$S(\nu) = \sum_{n=1}^{+\infty} \frac{\nu}{n(n-\nu)}$$

.

(II)

$$\mathbf{D}_t^{\nu_1}(\rho_1 u) - \mathbf{D}_t^{\nu_2}(\rho_2 u) = \mathbf{D}_t^{\nu_1}(\rho u) + \frac{\partial}{\partial t}(\mathcal{N}_{\nu_1,\nu_2} \star u),$$

where

$$\mathcal{N}_{\nu_1,\nu_2} = \varrho_2(x,t)\left[\frac{t^{-\nu_1}}{\Gamma(1-\nu_1)} - \frac{t^{-\nu_2}}{\Gamma(1-\nu_2)}\right] \geq 0,$$

if $t \in [0, T_{\nu_1}]$.
Thus we can exploit the key inequality (8).

Lemma 1

Let $\mathcal{K} \in C^1([0,T])$, $n \geq 2$, $p > \max\{n + \frac{2}{\nu_1}; \frac{1}{\nu_1 - \nu_2}\}$,
$\nu_1 \in (0,1)$; and let ν_2 satisfy **H1**.
We require that assumptions **H2-H6** hold.
Then the classical solution $u \in C^{2+\alpha, \frac{2+\alpha}{2}\nu_0}(\bar{\Omega}_T)$ of problem (1), (4)-(5) satisfies the estimate

$$\begin{aligned} &\|u\|_{\mathfrak{H}_p^{\nu_1,2}(\Omega_T)} + \|u\|_{C^{\alpha,\frac{\alpha\nu_1}{2}}(\bar{\Omega}_T)} + \|\mathbf{D}_t^{\nu_2} u\|_{L_p(\Omega_T)} \\ &\leq C\{\|f\|_{L_p(\Omega_T)} + \|u_0\|_{W^{2-\frac{2}{p\nu_1},p}(\Omega)} + \|\psi\|_{\mathfrak{H}_p^{\nu_1(1-\frac{1}{2p}),2-\frac{1}{p}}(\partial\Omega_T)}\}. \end{aligned} \tag{9}$$

Theorem 2

Let $\mathcal{K} \in C^1([0, T])$, $\psi \equiv 0$, $\partial\Omega \in C^{2+\alpha}$, parameters $p, n \geq 2, \nu_2, \nu_1$ satisfy conditions of Lemma 1, and **H2-H3**, **H5-H6** hold. We assume that

$$f \in L_p(\Omega_T) \cap W^{s_1,r}((0, T), W^{s_2,r}(\Omega)),$$

$$u_0 \in W^{2-\frac{2}{p\nu_1},p}(\Omega) \cap W^{2+s_2,r}(\Omega),$$

where $r \geq n+1$, $s_1 \in (r^{-1}, 1)$, $s_2 \in ((n+1)r^{-1}, 1)$.
Then for any fixed $T > 0$, linear IBVP (1), (4)-(5) admits a unique strong solution in the class $\mathfrak{H}_p^{\nu_1,2}(\Omega_T)$, satisfying estimate (9).

The similar results with $p = 2$ hold in the case of 1-dim under weaker assumptions: namely, $\mathcal{K} \in L_1(0, T)$ and without compatibility conditions.

Classical solvability to the semilinear equation

We obtain the one-to-one global classical solvability to Dirichlet and Neumann problem for

$$\sum_{j=1}^{N} \mathbf{D}_t^{\nu_j}(\rho_j u) - \mathcal{L}_1 u - \mathcal{K} \star \mathcal{L}_2 u = g(x,t) - f(u)$$

H7. Conditions on the nonlinearity: We assume that the function f satisfies the local Lipschitz condition, i.e. for every $\varrho > 0$, there exists a positive constant C_ϱ such that

$$|f(u_1) - f(u_2)| \leq C_\varrho |u_1 - u_2|$$

for any $u_1, u_2 \in [-\varrho, \varrho]$.
We assume also that the following inequality holds

$$|f(u)| \leq L(1 + |u|)$$

for some positive constant L and any $u \in R^1$.

$$\mathcal{K} \in \begin{cases} C^1([0,T]), & n \geq 2, \\ L_1(0,T), & n = 1 \end{cases}$$

.

Classical solvability to the nonlinear equation in 1dim.

We proved the existence of the unique strong solutions in the 1dim cases to the semilinear equation (i.e. (H7) holds).
Moreover, the classical and strong solvability are established in the case of $\rho_j \geq 0$ and
H8. Conditions on the nonlinearity:

$$\begin{cases} f \in C^1(R^1), \\ |f(u)| \leq \mathfrak{L}_1(1 + |u|^r), \\ uf(u) \geq -\mathfrak{L}_2 + \mathfrak{L}_3|u|^{r+1}, \\ f'(u) \geq -\mathfrak{L}_4, \end{cases}$$

for some nonnegative constants r and $\mathfrak{L}_i$, $i = 1, 2, 3, 4$.

Numerical examples

$$\mathbf{D}_t^{\nu} u + \frac{1}{2}\mathbf{D}_t^{\nu_1} u - \frac{1}{2}\mathbf{D}_t^{\nu_2} u - (t + \cos\frac{\pi x}{4})\frac{\partial^2 u}{\partial x^2} + (x+t)\frac{\partial u}{\partial x}$$
$$- \mathcal{K} \star b\frac{\partial^2 u}{\partial x^2} = f(x,t,u) \quad x \in (0,1), \quad t \in (0,1);$$

where

$$\mathcal{K} = t^{-1/3}, \qquad b = t^{1/3} + \sin\pi x, \qquad f(x,t,u) = xt\cos u^2,$$

$+$ the homogeneous Neumann boundary conditions at $x = 0$ and $x = 1$,

$$u(x,0) = \cos\pi x, \qquad x \in (0,1).$$

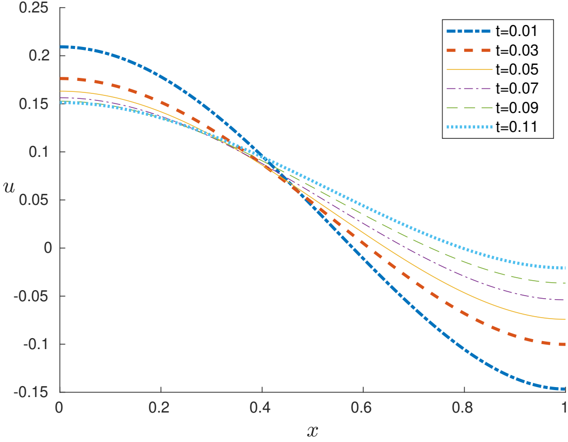

Figure: $\nu = 0.2, \nu_1 = \nu/3, \nu_2 = \nu/2$

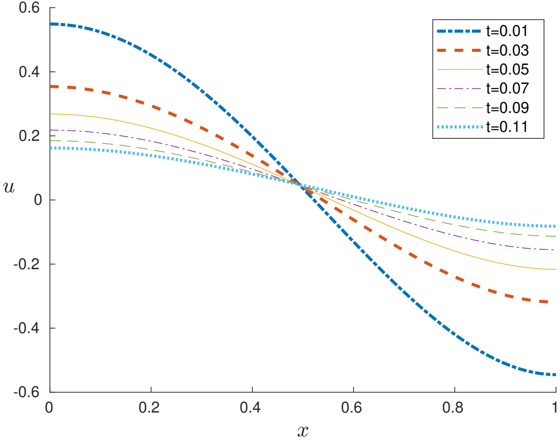

Figure: $\nu = 0.6, \nu_1 = \nu/3, \nu_2 = \nu/3$

Conclusions

- global classical solvability to IBVP for the linear version of (1) without assumptions on the sign of ρ_j, $j = 2, ..., N$, for all type boundary conditions
- existence and uniqueness of global strong solutions to IBVP for the linear version of (1) in the case of Dirichlet and Neumann BC, under additional consistency conditions if $n \geq 2$, and without them if $n = 1$
- classical global solvability of IBVP $(n \geq 1)$ to:
  - semilinear (1) if some ρ_j are negative;
  - nonlinear (1) if all ρ_j are non-negative
- existence and uniqueness of the strong solutions of IBVP (in 1d case) to
  - semilinear (1) if some ρ_j are negative;
  - nonlinear (1) if all ρ_j are non-negative
- numeric solutions

Open problems

- IBVP to the degenerate equations: $\rho_1 \to 0$ at either the boundary or a part of boundary or internal points or sets.
- Strong solvability of IBVP to the linear version of (1) in multidimensional case without assumptions on the consistency conditions.
- Existence and uniqueness of a strong solution of IBVP to nonlinear (1) if $n \geq 2$.
- Asymptotic behavior of solutions as $t \to +\infty$
- well-posedness in the case fully nonlinear equations like (1)
- Inverse problem, in particular, finding the coefficients ϱ_j and the order ν_j.

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- V. Pata, S.V. Siryk, N. Vasylyeva, *Multi-term fractional linear equations modeling oxygen subdiffusion through capillaries*, appear in Differential and Integral Equations, 2023.
- S.V. Siryk, N. Vasylyeva, *Initial-boundary value problems to semilinear multi-term fractional differential equations,* Communications on Pure and Applied Analysis, **22**(7) (2023) 2321-–2364.
- N. Vasylyeva, *Cauchy-Dirichlet problem to semilinear multi-term fractional differential equations,* Fractal Fractional, **7**(3) (2023) 249.

List of publications concerning to the project

Papers:

- S.V. Siryk, N. Vasylyeva, *Initial-boundary value problems to semilinear multi-term fractional differential equations,* Communications on Pure and Applied Analysis, **22**(7) (2023) 2321-–2364.
- N. Vasylyeva, *Cauchy-Dirichlet problem to semilinear multi-term fractional differential equations,* Fractal Fractional, **7**(3) (2023) 249.
- M. Chugunova, R. Taranets, N. Vasylyeva, *Initial-boundary value problems for conservative Kimura-type equations solvability asymptotic and conservation law,* J. Evol. Equ., **23**(1) (2023) 17.

Preprints:

- M. Chugunova, R. Taranets, N. Vasylyeva, Qualitative analysis of solutions for a degenerate PDE model of epidemic dynamics, https://doi.org/10.48550/arXiv.2207.11373, 2022. (submitted)
- S.V. Siryk, N. Vasylyeva, Initial-boundary value problems to semilinear multi-term fractional differential equations, https://doi.org/10.48550/arXiv.2301.07574, 2023.

THANK YOU FOR YOUR ATTENTION!