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Foreword

It is with great pleasure that we present the Proceedings of the 26th Congress of Differential Equations and Applications / 16th Congress of Applied Mathematics (XXVI CEDYA / XVI CMA), the biennial congress of the Spanish Society of Applied Mathematics S$\vec{e}$MA, which is held in Gijón, Spain from June 14 to June 18, 2021.

In this volume we gather the short papers sent by some of the almost three hundred and twenty communications presented in the conference. Abstracts of all those communications can be found in the abstract book of the congress. Moreover, full papers by invited lecturers will shortly appear in a special issue of the S$\vec{e}$MA Journal.

The first CEDYA was celebrated in 1978 in Madrid, and the first joint CEDYA / CMA took place in Málaga in 1989. Our congress focuses on different fields of applied mathematics: Dynamical Systems and Ordinary Differential Equations, Partial Differential Equations, Numerical Analysis and Simulation, Numerical Linear Algebra, Optimal Control and Inverse Problems and Applications of Mathematics to Industry, Social Sciences, and Biology. Communications in other related topics such as Scientific Computation, Approximation Theory, Discrete Mathematics and Mathematical Education are also common.

For the last few editions, the congress has been structured in mini-symposia. In Gijón, we will have eighteen minis-symposia, proposed by different researchers and groups, and also five thematic sessions organized by the local organizing committee to distribute the individual contributions. We will also have a poster session and ten invited lectures. Among all the mini-symposia, we want to highlight the one dedicated to the memory of our colleague Francisco Javier "Pancho" Sayas, which gathers two plenary lectures, thirty-six talks, and more than forty invited people that have expressed their wish to pay tribute to his figure and work.

This edition has been deeply marked by the COVID-19 pandemic. First scheduled for June 2020, we had to postpone it one year, and move to a hybrid format. Roughly half of the participants attended the conference online, while the other half came to Gijón. Taking a normal conference and moving to a hybrid format in one year has meant a lot of efforts from all the parties involved. Not only did we, as organizing committee, see how much of the work already done had to be undone and redone in a different way, but also the administration staff, the scientific committee, the mini-symposia organizers, and many of the contributors had to work overtime for the change.

Just to name a few of the problems that all of us faced: some of the already accepted mini-symposia and contributed talks had to be withdrawn for different reasons (mainly because of the lack of flexibility of the funding agencies); it became quite clear since the very first moment that, no matter how well things evolved, it would be nearly impossible for most international participants to come to Gijón; reservations with the hotels and contracts with the suppliers had to be cancelled; and there was a lot of uncertainty, and even anxiety could be said, until we were able to confirm that the face-to-face part of the congress could take place as planned.

On the other hand, in the new open call for scientific proposals, we had a nice surprise: many people that would have not been able to participate in the original congress were sending new ideas for mini-symposia, individual contributions and posters. This meant that the total number of communications was about twenty percent greater than the original one, with most of the new contributions sent by students.

There were almost one hundred and twenty students registered for this CEDYA / CMA. The hybrid format allows students to participate at very low expense for their funding agencies, and this gives them the opportunity to attend different conferences and get more merits. But this, which can be seen as an advantage, makes it harder for them to obtain a full conference experience. Alfréd Rényi said: "a mathematician is a device for turning coffee into theorems". Experience has taught us that a congress is the best place for a mathematician to have a lot of coffee. And coffee cannot be served online.

In Gijón, June 4, 2021

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Well posedness and numerical solution of kinetic models for angiogenesis

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Abstract

Angiogenesis processes including the effect of stochastic branching and spread of blood vessels can be described coupling a (nonlocal in time) integrodifferential kinetic equation of Fokker-Planck type with a diffusion equation for the angiogenic factor. Well posedness studies underline the importance of preserving positivity when constructing approximate solutions. We devise order one positivity preserving schemes for a reduced model and show that soliton-like asymptotic solutions are correctly captured. We also find good agreement with the original stochastic model from which the deterministic kinetic equations are derived working with ensemble averages. Higher order positivity preserving schemes can be devised combining WENO and SSP procedures.

1. Angiogenesis model

Angiogenesis (growth of blood vessels) is fundamental for tissue repair and development. A host of immune, inflammatory and malignant diseases are triggered by angiogenic disorders. We study here a deterministic integrodifferential model for the development of the stochastic vessel network.

Denoting by p and C the density of blood vessel tips and the concentration of angiogenic factor released by hypoxic cells, their time evolution is governed by a system of nondimensional equations [1]:

$$\begin{aligned}\frac{\partial}{\partial t}p(\mathbf{x},\mathbf{v},t) &= \alpha(C(\mathbf{x},t))\delta_{\sigma_v}(\mathbf{v}-\mathbf{v}^0)p(\mathbf{x},\mathbf{v},t) - \Gamma p(\mathbf{x},\mathbf{v},t)\int_0^t ds\int d\mathbf{v}' p(\mathbf{x},\mathbf{v}',s)\\ &\quad -\mathbf{v}\cdot\nabla_{\mathbf{x}}p(\mathbf{x},\mathbf{v},t)+\beta\,\mathrm{div}_{\mathbf{v}}(\mathbf{v}p(\mathbf{x},\mathbf{v},t))+\\ &\quad -\mathrm{div}_{\mathbf{v}}\left[\beta\mathbf{F}\left(C(\mathbf{x},t)\right)p(\mathbf{x},\mathbf{v},t)\right]+\frac{\beta}{2}\Delta_{\mathbf{v}}p(\mathbf{x},\mathbf{v},t), \qquad (1.1)\\ \frac{\partial}{\partial t}C(\mathbf{x},t) &= \kappa\Delta_{\mathbf{x}}C(\mathbf{x},t)-\chi C(\mathbf{x},t)j(\mathbf{x},t), \qquad (1.2)\\ p(\mathbf{x},\mathbf{v},0) &= p_0(\mathbf{x},\mathbf{v}), \quad C(\mathbf{x},0)=C_0(\mathbf{x}), \qquad (1.3)\end{aligned}$$

where

$$\alpha(C(\mathbf{x},t)) = A\frac{C(\mathbf{x},t)}{1+C(\mathbf{x},t)}, \quad \mathbf{F}(C(\mathbf{x},t)) = \frac{\delta_1}{(1+\Gamma_1 C(\mathbf{x},t))^{q_1}}\nabla_{\mathbf{x}}C(\mathbf{x},t), \qquad (1.4)$$

$$j(\mathbf{x},t) = \int_{\mathbb{R}^N}\frac{|\mathbf{v}|}{1+e^{(|\mathbf{v}-\mathbf{v}^0|^2-\eta)/\epsilon}}p(\mathbf{x},\mathbf{v},t)\,d\mathbf{v}, \quad \rho(\mathbf{x},t)=\int_{\mathbb{R}^N}p(\mathbf{x},\mathbf{v},t)\,d\mathbf{v}, \qquad (1.5)$$

for $\mathbf{x}\in\Omega\subset\mathbb{R}^N$, $\mathbf{v}\in\mathbb{R}^N$, $N=2,3$, $t\in[0,\infty)$. The parameters β, Γ, κ, χ, A, Γ_1, δ_1, η, ϵ and q_1 are dimensionless and positive. Typical values are listed in Table 1. Here, δ_{σ_v} is a regularized delta function, such as

$$\delta_{\sigma_v}(\mathbf{v}-\mathbf{v}_0) = \frac{1}{\pi\sigma_v^2}\,e^{-|\mathbf{v}-\mathbf{v}_0|^2/\sigma_v^2}. \qquad (1.6)$$

In dimension two, these models can be adapted to describe angiogenesis problems causing retinopathies [2].

δ_1	β	A	Γ	Γ_1, q_1	κ	χ	η	ϵ	σ_v
0.255	5.88	22.42	0.135	1	0.0045	0.002	15	0.001	0.08

Tab. 1 Dimensionless parameters.

Existence, uniqueness and stability of positive solutions is established in the whole space resorting to iterative procedures. The key idea for an existence theory is to include the integrodifferential terms in the reference linear operators [3]: we consider iterative schemes in which the velocity integrals ρ and j are fixed from one step to the next. Then, we construct solutions of the linearized Fokker-Plank and heat problems by means of fundamental solutions. This guarantees nonnegativity of the solutions, a crucial property to obtain preliminary uniform estimates. Existence follows from compactness arguments, using sharp estimates on the force field $\mathbf{F}(C)$ and on the anastomosis terms. Passing to the limit in the equations, we obtain a global in time solution of the original problem for initial data decaying at infinite, as well as stability bounds in terms of the norms of the initial data. Gronwall type inequalities yield uniqueness. More precisely, the following result is proven in [3]

Theorem 1. *Let us assume that:*

$$p_0 \geq 0, C_0 \geq 0, \tag{1.7}$$
$$C_0 \in L^\infty(\boldsymbol{R}^N), \nabla_{\mathbf{x}} C_0 \in L^\infty(\boldsymbol{R}^N) \cap L^2(\boldsymbol{R}^N), \tag{1.8}$$
$$(1+|\mathbf{v}|^2)^{\beta/2} p_0 \in L^\infty(\boldsymbol{R}^N \times \boldsymbol{R}^N), \quad \beta > N, \tag{1.9}$$
$$(1+|\mathbf{v}|^2)^{\beta/2} p_0 \in L^1(\boldsymbol{R}^N \times \boldsymbol{R}^N), \quad \beta > N. \tag{1.10}$$

Then, there exists a nonnegative solution (p, C) of (1.1)-(1.5) satisfying:

$$C \in L^\infty(0,T; L^\infty(\boldsymbol{R}^N)), \nabla_{\mathbf{x}} C \in L^\infty(0,T; L^\infty \cap L^2(\boldsymbol{R}^N)), \tag{1.11}$$
$$p \in L^\infty(0,T; L^\infty \cap L^1(\boldsymbol{R}^N \times \boldsymbol{R}^N)), \nabla_{\mathbf{v}} p \in L^2(0,T; L^2(\boldsymbol{R}^N \times \boldsymbol{R}^N)), \tag{1.12}$$
$$(1+|\mathbf{v}|^2)^{\beta/2} p \in L^\infty(0,T; L^\infty(\boldsymbol{R}^N \times \boldsymbol{R}^N)), \tag{1.13}$$
$$(1+|\mathbf{v}|^2)^{\beta/2} p \in L^\infty(0,T; L^1(\boldsymbol{R}^N \times \boldsymbol{R}^N)), \tag{1.14}$$
$$p \in L^\infty(0,T; L^\infty_{\mathbf{x}}(\boldsymbol{R}^N, L^1_{\mathbf{v}}(\boldsymbol{R}^N)), \tag{1.15}$$

with norms bounded in terms of the norms of the data.
If $\nabla_{\mathbf{v}} p_0 \in L^\infty_{\mathbf{x}}(\boldsymbol{R}^N, L^1_{\mathbf{v}}(\boldsymbol{R}^N))$, then $\nabla_{\mathbf{v}} p \in L^\infty(0,T; L^\infty_{\mathbf{x}}(\boldsymbol{R}^N, L^1_{\mathbf{v}}(\boldsymbol{R}^N))$ and the solution is unique.

When the spatial domain Ω is bounded, we need to impose boundary conditions. We consider the slab $(0, L) \times \mathbb{R}$, and set $\mathbf{x} = (x_1, x_2)$, $\mathbf{v} = (v_1, v_2)$. On $x_1 = 0$ (initial blood vessel) and $x_1 = L$ (hypoxic region), we impose Neumann boundary conditions for C:

$$\frac{\partial}{\partial \mathbf{n}} C(0, x_2, t) = 0, \quad \frac{\partial}{\partial \mathbf{n}} C(L, x_2, t) = c_L(t) e^{-a^2 x_2^2}, \quad t > 0, x_2 \in \mathbb{R}, \tag{1.16}$$

where $c_L(t) > 0$ represents the influx of angiogenic factor produced at the hypoxic region and $1/a$ is a characteristic length. This function decreases as blood vessels reach the hypoxic region. We impose nonlocal boundary conditions hold on p:

$$p^+(0, x_2, v_1, v_2, t) = \frac{e^{-|\mathbf{v}-\mathbf{v}_0|^2}}{\int_0^\infty \int_{-\infty}^{+\infty} v_1' \, e^{-|\mathbf{v}'-\mathbf{v}_0|^2} dv_1' dv_2'} \Big[j_0(x_2, t)$$
$$- \int_{-\infty}^0 \int_{-\infty}^{+\infty} v_1' \, p^-(0, x_2, v_1', v_2', t) dv_1' dv_2' \Big] = S_0(p), \quad t, v_1 > 0, v_2, x_2 \in \boldsymbol{R}, \tag{1.17}$$
$$p^-(L, x_2, v_1, v_2, t) = \frac{e^{-|\mathbf{v}-\mathbf{v}_0|^2}}{\int_{-\infty}^0 \int_{-\infty}^{+\infty} e^{-|\mathbf{v}'-\mathbf{v}_0|^2} dv_1' dv_2'} \Big[\rho_L(x_2, t)$$
$$- \int_0^{+\infty} \int_{-\infty}^{+\infty} p^+(L, x_2, v_1', v_2', t) dv_1' dv_2' \Big] = S_L(p), \quad t > 0, v_1 < 0, x_2, v_2 \in \boldsymbol{R}, \tag{1.18}$$

where p^+ denotes the values of p for positive v_1 and p^- the values of p for negative v_1. For a fixed $\mathbf{v}_0 = (v_{1,0}, v_{2,0})$

$$j_0(x_2, t) = v_{1,0} \, \alpha(C(0, x_2, t)) \, p(0, x_2, v_{1,0}, v_{2,0}, t), \tag{1.19}$$
$$\rho_L(x_2, t) = \rho(L, x_2, t) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} p(L, x_2, v_1', v_2', t) dv_1' dv_2'. \tag{1.20}$$

Existence results are based on similar iterative schemes as those employed in the whole space. However, lacking explicit fundamental solutions, proofs exploit balance equations, estimates of velocity decay and compactness results for kinetic operators, combined with gradient estimates of heat kernels for Neumann problems (see [4] for detailed proofs of existence results in an annulus).

We aim to devise robust schemes for this kind of problems. In principle, we could rely on the iterative schemes used for existence, and apply schemes for linear kinetic and heat equations to each iterate. However, the convergence of the iterative scheme may be slow and the order of the resulting procedure would be uncontrolled. Instead, we will discuss how to discretize the original nonlinear problem. To simplify, we will illustrate the ideas on a two dimensional reduction that captures soliton-like solutions. Section 2 describes the discretization procedure. Section 3 presents some numerical results.

2. Positivity preserving high order schemes

In the limit as $\beta \to \infty$, the marginal density $\rho(\mathbf{x}, t)$ and the concentration satisfy the equations [1]:

$$\frac{\partial \rho}{\partial t} + \mathrm{div}_{\mathbf{x}}(\mathbf{F}\rho) - \frac{1}{2\beta}\Delta_{\mathbf{x}}\rho = \mu\,\rho - \Gamma\rho \int_0^t \rho(\mathbf{x}, s)\, ds, \tag{2.1}$$

$$\mu = \frac{\alpha}{\pi}\left[1 + \frac{\alpha}{2\pi\beta(1+\sigma_v^2)} \ln\left(1 + \frac{1}{\sigma_v^2}\right)\right], \tag{2.2}$$

$$\frac{\partial}{\partial t} C(\mathbf{x}, t) = \kappa \Delta_{\mathbf{x}} C(\mathbf{x}, t) - \chi_1\, C(\mathbf{x}, t)\, \rho(\mathbf{x}, t), \tag{2.3}$$

$$\chi_1 = \frac{\chi}{\pi} \int_0^{\infty} \int_{-\pi}^{\pi} \frac{\sqrt{1 + V^2 + 2V\cos\varphi}}{1 + e^{(V^2-\eta)/\epsilon}} e^{-V^2} V\, dV d\varphi. \tag{2.4}$$

To leading order, the density and the marginal density are related by

$$p(\mathbf{x}, \mathbf{v}, t) \sim \frac{1}{\pi} e^{-|\mathbf{v}-\mathbf{v}_0|^2} \rho(\mathbf{x}, t). \tag{2.5}$$

A positivity preserving order one scheme follows by explicit forward time discretization, upwind treatment of transport terms, and standard centered schemes for the Laplacians. Integral terms are discretized by means of composite Simpson rules. The integral $I(\mathbf{x}, t) = \int_0^t \rho(\mathbf{x}, s)\, ds$ is transformed in an additional equation

$$I'(\mathbf{x}, t) = \rho(\mathbf{x}, t), \quad I(\mathbf{x}, 0) = 0. \tag{2.6}$$

To obtain a higher order scheme, we apply a positivity preserving WENO5 scheme to spatial operators, combined with three point Legendre quadrature rules [7]. In spite of their order, these schemes may degenerate to order two in practice. To preserve positivity and stability, we consider strong stability preserving (SSP) time discretizations. Standard choices for third order accuracy are the third order SSP multistep method [7]

$$u(t_{n+1}) = \tfrac{16}{27}\left(u(t_n) + 3\delta t\, r(u(t_n))\right) + \tfrac{11}{27}\left(u(t_{n-3}) + \tfrac{12}{11}\delta t\, r(u(t_{n-3}))\right), \tag{2.7}$$

and the third order Runge Kutta method [6]

$$\begin{aligned} u^{(1)} &= u(t_n) + \delta t\, r(u(t_n)), \\ u^{(2)} &= \tfrac{3}{2}u(t_n) + \tfrac{1}{4}u^{(1)} + \tfrac{1}{4}\delta t\, r(u^{(1)}), \\ u(t_{n+1}) &= \tfrac{1}{3}u(t_n) + \tfrac{2}{3}u^{(2)} + \tfrac{2}{3}\delta t\, r(u^{(2)}). \end{aligned} \tag{2.8}$$

The stability of SSP methods is governed by a CFL number c in the following way. If the Euler forward time discretization applied to an equation $u_t = r(u)$ is stable under the condition $\delta t \leq \delta t_0$, then the higher order SSP time discretization is stable when $\delta t \leq d\, \delta t_0$. For the multistep method we have $d = 1/3$ while $d = 1$ ($d_{eff} = 1/3$) for the RK3 (2.8). For second order accuracy, the RK2 scheme is

$$\begin{aligned} u^{(1)} &= u(t_n) + \delta t\, r(u(t_n)), \\ u(t_{n+1}) &= \tfrac{1}{2}u(t_n) + \tfrac{1}{2}u^{(1)} + \tfrac{1}{2}\delta t\, r(u^{(1)}) \end{aligned} \tag{2.9}$$

with $d = 1$ ($d_{eff} = 1/2$). The spatial operator $r(u(t_n))$ would be the operator obtained discretizing the space variables, time excluded. These schemes can be extended to the whole model [5].

3. Numerical results

In this section, we present numerical solutions for appropriate values of the parameters as listed in Table 1.

Figure 1 shows the evolution of the marginal tip density (1.5) at four different times as the angiogenic network moves towards the hypoxic region on the right, obtained by combining a WENO5 discretization in space and RK2 in time. Figures 2 depicts the angiogenic factor concentration. We observe that the active vessel tips evolve as a patch as they consume the concentration of theangiogenic factor as they advance. The tip density profile forms a soliton-like pattern, with slightly varying profile. The soliton forms at the initial stage and then advances keeping its appearance but changing its size and height. This numerically observed soliton can be described asymptotically as explained in [1].

Acknowledgements

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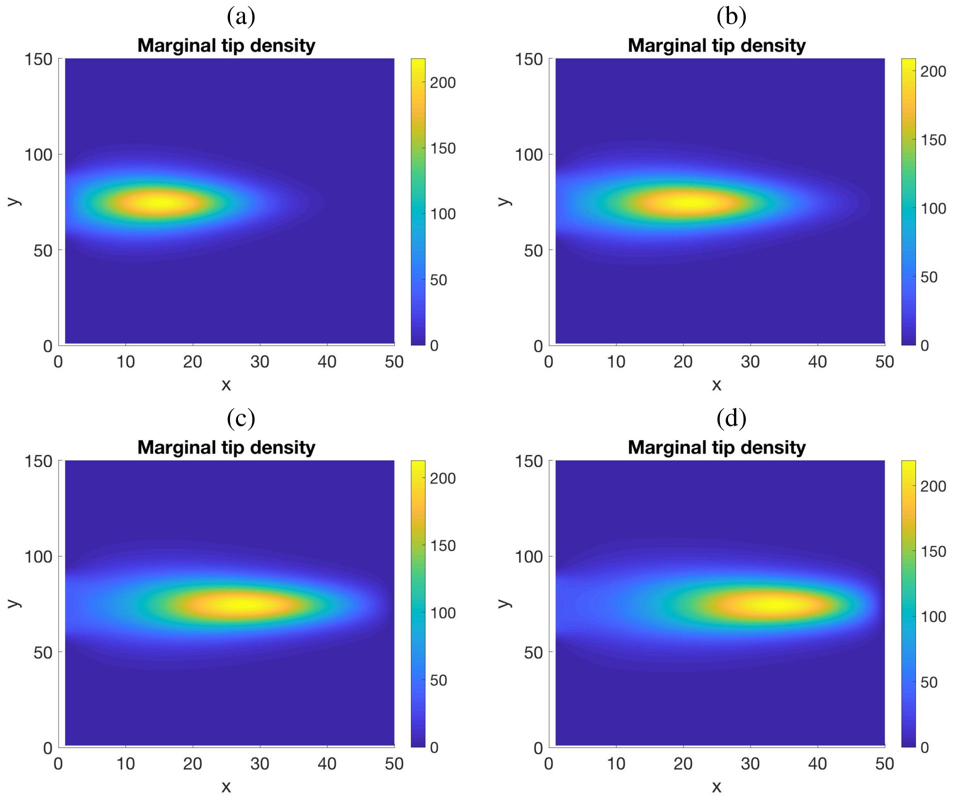

Fig. 1 Snapshots of the time evolution of the marginal tip density.

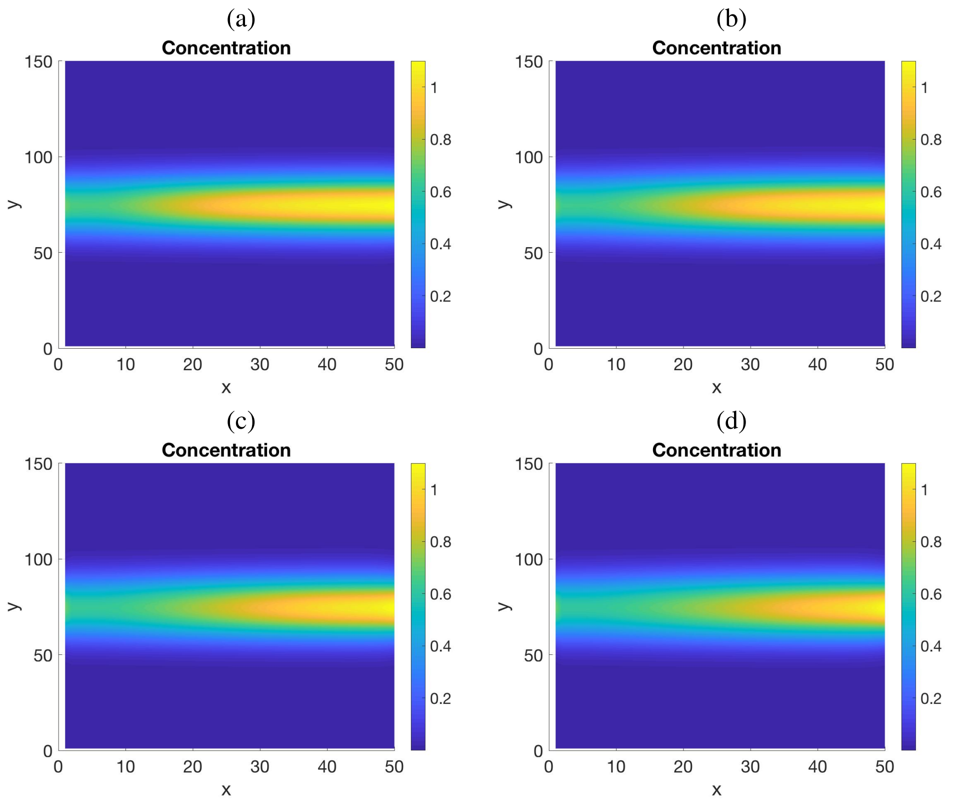

Fig. 2 Snapshots of the time evolution of the concentration.

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