# HUMAN DIGITAL TWINS: MULTISCALE MODELING AND SIMULATIONS OF CELL DYNAMICS

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In the last years, the concept of digital twins is attracting the interests of different research fields. In particular human digital twins represent a promising tool to build customizable models of organs, and a way to simulate biological phenomena in order to predict outcomes, avoiding unnecessary surgery and reducing the costs of laboratory experiments. In this talk recent results on mathematical models inspired by Organ-on-chip experiments will be presented. The focus will be on a hybrid differential model for cell migrations due to mechanical and chemical interaction. Starting from the microscopic scale, numerical simulations of the derived kinetic and macroscopic models will be presented.

**Keywords**: *mathematical biology, cell migration, differential models, human digital twins*

## 1. Outline

Human digital twins represent an increasingly promising strategy to provide methods of analyzing healthcare practices. The complexity of human organisms and the difficult biological mechanism of systems within the human body are still challenging aspects of the building process.

In this talk we focus on a general class of hybrid mathematical models designed for collective motions of cells due to chemical stimuli, describing the behavior of immune cells and the concentration of chemicals in Cancer-on-chip environment [1]. In this context, cells are modeled as discrete entities and their dynamics is given by ODEs, while the chemical signal influencing the motion is considered as a continuous signal which solves a diffusive equation. The generical structure of the hybrid approach envisaged can be summarized as follows: consider on $\mathbb{R}^{2dN} \ni ((x_i(t))_{i=1,\dots,N}, (v_i(t))_{i=1,\dots,N}) := (X(t), V(t))$ the following vector field

$$\begin{cases} \dot{x_i}(t) = v_i \\ \dot{v_i}(t) = F_i(t, X(t), V(t)) \end{cases} \qquad i = 1, \dots, N, \tag{1}$$

where

$$F_i(t, X, V) = \sum_{j=1}^{N} \gamma(v_i - v_j, x_i - x_j) + \eta \nabla_x \varphi^t(x_i) \tag{2}$$

Here $x_i, v_i$ are the position and velocity of the i-th cell, function $\gamma$ models the mechanical interactions among cells and $\varphi$ stands for a generic chemical signal produced by the cells themselves and such that the cells are attracted towards the direction where $\nabla_x \varphi$ is growing. In particular, $\varphi$ satisfies the equation

$$\partial_s \varphi^s(x) = D\Delta_x \varphi - \kappa\varphi + f(x, X(s)), \ s \in [0, t], \tag{3}$$

for some $\kappa, D, \eta \geq 0$ and function $f$ of the form

$$f(x, X) = \frac{1}{N} \sum_{j=1}^{N} \chi(x - x_i), \ \ \chi \in \mathcal{C}_c^1. \tag{4}$$

Numerical and analytical results on hybrid models in a two-dimensional domain ($d = 2$) can be found in [2], whereas application to Cancer-on-chip experiments in [3].

The final goal of building digital twins is to predict the behaviour of real organs, hence on the scale of billions of cells, using the data from the Organ-on-chip experiments. To this end, it is crucial to design a macroscopic model, which allows to overcome the computation complexity of a microscopic approach, keeping the microscopic experimental information.

From the analytical point of view, a pressureless nonlocal Euler-type system has been derived for the class of model (1)-(2), and a rigorous equivalence between kinetic and macroscopic scale has been proved assuming monokinetic initial data [4]. Denoting with $\mu$ the macroscopic density, and $u$ the velocity field, the system reads:

$$\begin{cases} \partial_t \mu^t + \nabla(u^t \mu^t) = 0 \\ \\ \partial_t(\mu^t u^t) + \nabla(\mu^t (u^t)^{\otimes 2}) = \mu^t \int \gamma(\cdot - y, u^t(\cdot) - u^t(y))\mu^t(y)dy + \eta \mu^t \nabla \psi^t - \alpha \mu^t u^t \\ \\ \partial_s \psi^s = D\Delta\psi - \kappa\psi + \chi * \mu^s, \ s \in [0, t], \end{cases}$$

Concerning generic and more realistic initial configurations, a numerical study has been performed [5], as a first step in the study of the model at different scale. Two main aspects will be debated: the difference with respect to Euler system of equation accounting for pressure, and the role of the non-local integral term. Numerical simulations, investigating the role of key parameters of the model in different scenarios, will be shown. In particular, a comparison between microscopic, kinetic and macroscopic scale will be highlighted.

This talk is based on joint works and ongoing collaborations in particular with Gabriella Bretti, Roberto Natalini (IAC-CNR) and Thierry Paul (CNRS-Sorbonne Universitè) .

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