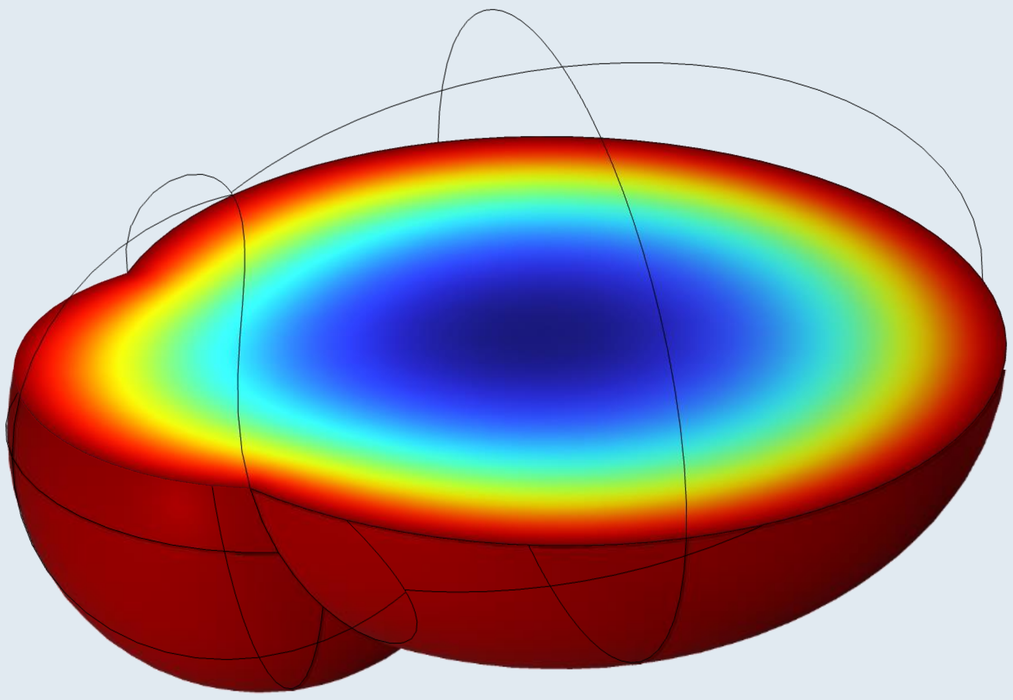

# Modeling Oxygen Metabolism in 3D Cell Constructs with LiveLink™ for MATLAB®

A novel approach to empower Finite Element Models (FEMs) for high throughput in silico experiments on spheroids and organoids.

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## Introduction

**Oxygen ($O_2$) metabolism** plays a key role in cellular function [1]. Alterations in metabolism are often related to dysfunction and disease [2].

FEMs are exploited for studying $O_2$ and nutrient dynamics in a **continuum domain**. Hence, they cannot exhaustively describe metabolism in 3D cell constructs [3, 4, 5], which are constituted of **consuming discrete units** at the microscale (*i.e.*, cells) embedded in **non-consuming extracellular space**.

We exploited the COMSOL® **LiveLink™ for MATLAB®** to develop the **Nebuloid** and **Genoid**, enabling the description of cell-scale metabolic dynamics and prediction of construct morphologies compliant with biophysical constraints, respectively.

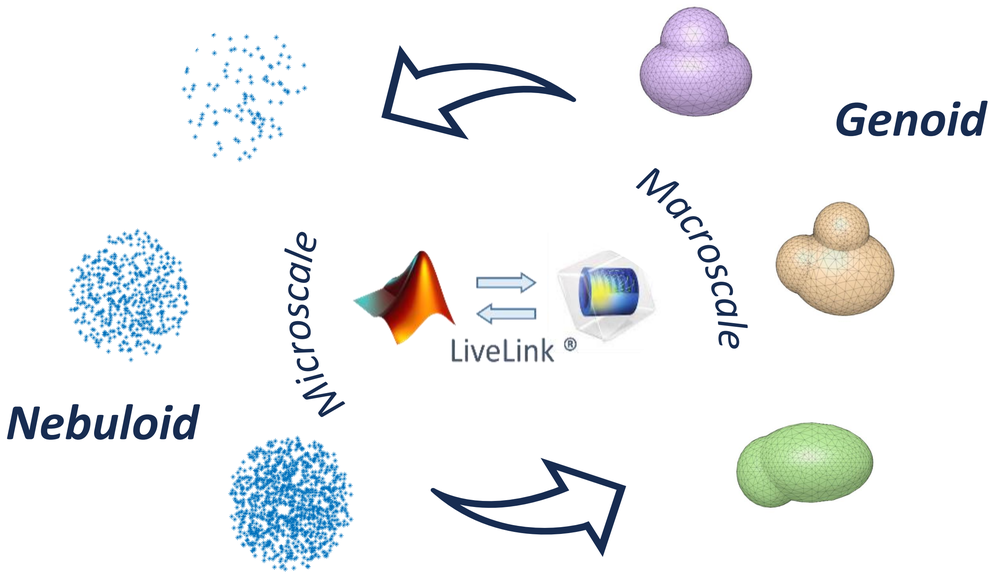



Figure 1. Graphical workflow

## Methodology

1. The Nebuloid is an agent-based model [6], implemented as a **random point cloud** representing homogeneously distributed cells within the construct volume. This allows modelling their metabolism at the **single-cell** scale.

2. The Evolvoid iteratively runs FEMs simulating $O_2$ diffusion-reaction in cell constructs. Based on the solutions obtained, their shape is refined to comply with **biophysical constraints** (*e.g.*, optimized oxygen supply) using **genetic algorithms** (GAs) [7].

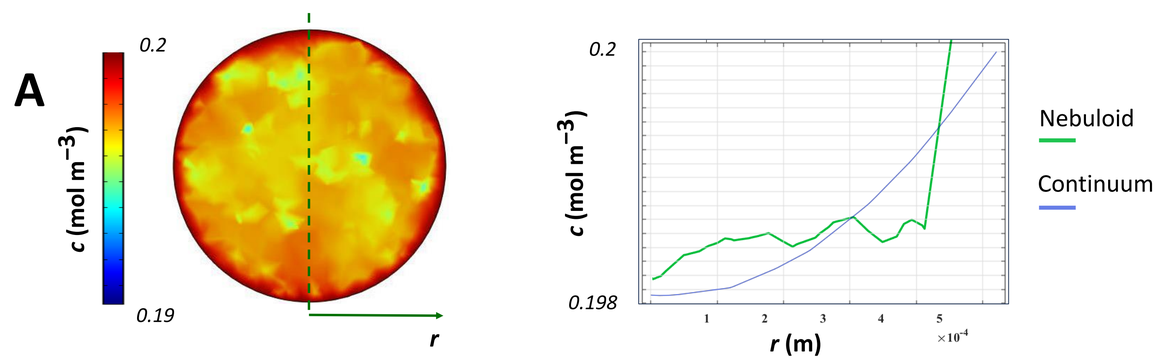
In both the approaches, **Transport of Diluted Species** is used to solve the steady-state diffusion-reaction of **$O_2$**.

## Results & Future Perspective

1. Nebuloid and classic continuum models differ regarding the predicted **$O_2$ concentration field** (Figure 2A). This also implies discrepancies in terms of the construct **metabolic rate** (MR, *i.e.*, the rate of $O_2$ consumption in mol/s) (Figure 2B).

2. The Genoid framework enables the identification of **optimal morphologies** according to a fitness function based on biophysical constraints.

The **integration** of the Nebuloid with the Genoid and their **experimental validation** are ongoing to provide a cost-effective and sustainable **lab on a laptop** for studying metabolic processes in human-relevant pathophysiology.



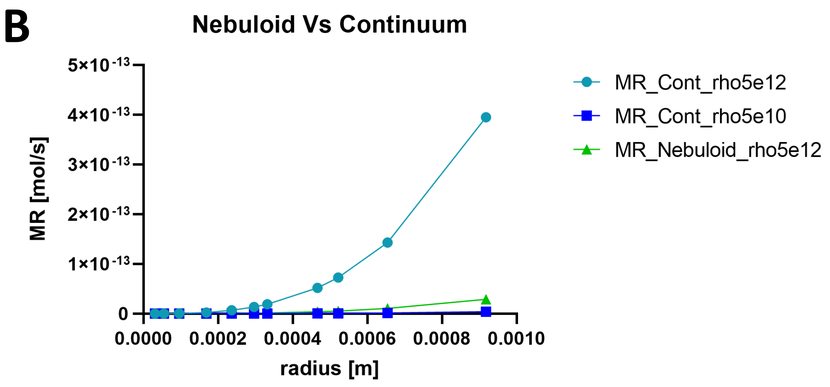




Figure 2. Comparison between the Nebuloid and the continuum model in terms of: A) $O_2$ concentration field; B) MR as a function of the construct radius

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