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Nebuloid: a novel *in silico* agent-based cell model

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Proliferation and resource consumption of cells are predicted using a classic continuum approach in *in silico* models. For instance, in a 3D cell-laden spheroid consuming oxygen, the construct is represented as a unique finite domain through which oxygen flux is governed by the diffusion and consumption equation. Although this approach is widely used for several applications, it has some limitations. As a matter of fact, encapsulated cells in 3D structures are composed of discrete consuming units within extracellular non consuming space. Thus, *in silico* models assume consumption in all the nodes of the mesh (*i.e.*, the domain where the physics applies) using an estimated cell density. Moreover, they do not take into account the real arrangement of the cells within the construct or consider any regions occupied by extracellular matrix and do not attribute cell-specific metabolic parameters, which do in fact change with phenotype. Here, we propose an *in silico* model developed with the COMSOL Livelink environment for Matlab, where cells within the construct were modelled as a point cloud with a homogeneous spatial distribution. In the simplest model, the cells consume oxygen following the Michaelis-Menten equation, with the same metabolic parameters (sOCR and Km). The metabolic rate (B) was calculated as the inward flux at spheroid surface for spheres with different radius and same cell density (5.14e12 [cell/m3]). Preliminary results show discrepancies in the values of B between the bulk continuum model and the one obtained in the Nebuloid model developed here. Nebuloid allows control of the spatial position and the metabolic parameters for each cell: this is crucial for developing more relevant and predictive models for 3R approaches.

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