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A CHEMICO-MECHANICALLY INDUCED CELL MODEL WITH AN APPLICATION TO CANCER METASTASIS

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Summary: In many biomedical processes like wound healing, organ development and cancer metastasis, cells are migrating. Cell migration could be classified mainly into amoeboid movement and mesenchymal movement, which is necessary to for instance close a wound opening and is detrimental in many cases like cancer metastasis. When cancer cells are spreading, they are able to deform to fulfill penetration and this deformation is often driven by external signals such as chemotaxis, durotaxis or tensotaxis.

In our work, we develop a phenomenological model for chemico-mechanically induced cell and nucleus deformation with an application to cancer spread in 2D or/and 3D. Taking a generic signal into account, the emitting source has been incorporated such that it allows a simple treatment using Green's Fundamental solutions. Next to the signal, the interaction between the cell membrane and its nucleus proceeds via the stiffness of the cell's cytoskeleton, which is dealt with using a collection of springs. Furthermore, stochastic processes are considered to simulate the random movements of cell and nucleus. To determine the positions of one cell and its nucleus, we use an IMEX time-integration method to update the positions such that the linear parts are treated using an Euler backward scheme, whereas the nonlinear parts are treated in a forward Euler method. Since many of the input parameters are not know well, the quantification of the propagation of uncertainty in the data is crucially important. To this extent, we carry out Monte Carlo Simulation to estimate likelihoods of (cancer) cell penetration.

As far as we know, it will be the first description considering the interactive deformation between cell and its nucleus during cancer metastasis. Moreover, this cell-based model is able to quantify the influence of the stiffness of the cell nucleus to the deformability and its ability to migrate through narrow cavities. Therefore, the model is expected to predict the microenvironmental behavior of cell and nucleus and to aid biological experiments as well as clinical trials for researching cancer metastasis inhibition and new drug developments.