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Proliferation rate estimation using a continuum-mechanical cancer cell model

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Once lung-cancer cells have invaded the brain tissue via the blood-vessel system, the cells proliferate and migrate in the tissue. The nutrients in the interstitial fluid ensure the proliferation and the basal reactions of the cancer cells. Over time, the cancer cells proliferate and form metastases. In experiments, multicellular lung-cancer spheroids are grown under fully-nutrient-supplied conditions, which allow the comparison of the experiment to the early stage of the formation of lung-cancer metastases in a continuum-mechanical model. Moreover, the experiments enable the adaptation of relevant model parameters via maximum likelihood estimation.

In this contribution, the model is focused on the cancer-cell proliferation starting from an initial cancer cell amount within the tissue. Furthermore, the cells can spread within the brain tissue and, thus, increase the affected region.
As a consequence of the time series of the experimental data, the model is simulated for the same observation period, allowing for the comparison of the overall cancer-cell amount in space and time.

In this contribution, the continuum-mechanical model is based on the
Theory of Porous Media (TPM). Therein, the microscopic structure is volumetrically homogenised over a representative elementary volume leading to a macroscopic multi-phase model with interacting continua. In particular, the constituents are given by an elastic solid skeleton (brain cells) and two immiscible pore liquids (blood and interstitial fluid). Herein, the latter is a real mixture of the proliferating cancer cells and nutrients. The proliferation and consumption themselves are described via mass-production terms.

Numerically, the weak forms of the overall momentum balance and the adapted mass-balance relations are solved for their related primary variables. Thereby, the primary variables are the solid deformation, the pressures of the liquids as well as the concentrations of the cancer cells and the nutrients. The resulting coupled system of equations is solved monolithically applying the finite-element tool PANDAS. In this procedure, the spatial discretisation is realised via Taylor-Hood elements and the time is resolved on the basis of an Euler time-integration scheme.

Finally, the results are compared to the volumetric lung-cancer-cell data obtained from experiments. Thereby, an optimisation of the proliferation parameters is performed using the maximum likelihood estimation. This procedure leads to repeated executions of the numerical model and consequently to a better estimation of the proliferation rates.

References

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Primary authors: Mr SCHRÖDER, Patrick (Institute of Applied Mechanics (CE), University of Stuttgart); Dr WAGNER, Arndt (University of Stuttgart); Ms STÖHR, Daniela (University of Stuttgart, Institute of Cell Biology and Immunology); Mr REHM, Markus (Institute of Cell Biology and Immunology, University of Stuttgart); Ms JENSCH, Antje (Institute for Systems Theory and Automatic Control, University of Stuttgart); Ms RADDE, Nicole (Institute for Systems Theory and Automatic Control, University of Stuttgart); Mr EHLERS, Wolfgang (Institute of Applied Mechanics (CE), University of Stuttgart)

Presenter: Mr SCHRÖDER, Patrick (Institute of Applied Mechanics (CE), University of Stuttgart)

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