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Theoretical and experimental study of intracellular transport using a porous media approach

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Intracellular transport of macromolecules is essential to numerous biological functions, particularly for apoptosis (programmed cell death). During this process, specialised proteins called caspases are produced and transported within the cell. Their activity leads to the reorganisation of cytoplasmic structures, including the actin cytoskeleton. The rearrangement of this fibrous structure may in return alter the intracellular transport properties of caspases (effective diffusivity and reaction rates) and therefore their activity. To our knowledge, the impact of the cytoskeleton remodelling on the intracellular transport properties has remained largely unexplored.

Here we propose to combine porous media theory and cell biology experiments to study the coupling between the reorganisation of the actin cytoskeleton and the intracellular transport of large proteins. At the local scale, the cytoplasm is modelled as a nanometric fibrous porous medium surrounded by a homogeneous fluid. With a radius of 4 nm, the actin fibres typically form structures with a pore size ranging from 10nm to 100nm [2]. The diffusive particles considered have a nanometric radius, leading to significant tortuous and hydrodynamic diffusional hindrances [3]. A homogenisation procedure is carried using the Volume Averaging Method [4], allowing the determination of the relevant effective transport properties and cell scale transport equations. The link between actin structures (local scale) and effective transport properties (cell scale) is investigated by numerically solving closure problems arising from the procedure. Finally, the cell scale model is solved on specific cases for validation against experimental measurements inside living cells. Cytoplasmic diffusion of endogenously expressed fluorescent tracers is studied quantitatively using both Fluorescence Recovery After Photobleaching (FRAP) and Fluorescence Correlation Spectroscopy (FCS) techniques.

This multidisciplinary work may lead to a better understanding of diffusion-reaction processes in biological porous structures, with possible implications on apoptosis related disorders such as autoimmune diseases and cancer.

Participation

In-Person

References

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