JOB DESCRIPTION - DOCTORAL STUDENT

COMPONENT AND SERVICE CDD Dates :	INSTITUT PPRIME – UNIVERSITE DE POITIERS From 01/10/2025 to 31/09/2028 (36 months) Department / team : Department Mechanical Engineering and Complex Systems (GMSC), team Photomechanics and Experimental Mechanics
Thesis supervisors	Thesis Director : Germaneau Arnaud : arnaud.germaneau@univ-poitiers.fr Co-supervisor : Caillé Laetitia : laetitia.caille@univ-poitiers.fr
JOB TITLE POSITION LOCATION	Doctorant Contractuel SP2MI – 86360 CHASSENEUIL DU POITOU
Short title	A new inverse method approach for 3D identification: an extension to cellular biomechanics
DIPLOMAS	Master (Ingénierie de Conception, Mécanique, Mathématiques et Applications)
RESEARCH PROJECT	Nom : ANR InvABio n° Eotp : E397CR24

CONTEXT AND MISSION

The thesis is part of the ANR InvABio project. The context and description of the thesis subject can be found below.

DESCRIPTION OF THESIS SUBJECT

Background to the study and previous results:

Glioblastomas are the most common and aggressive brain tumours in adults. These tumours are characterised by the presence of invasive cells at their periphery that can disseminate into the surrounding brain tissue, which is responsible for their lethality associated with recurrence. The ability of glioblastoma cells to infiltrate brain tissue within the extracellular matrix (ECM) has been linked to the formation of invadopodia [1].

Essential to the invasive process, these membrane protuberances are micrometric structures capable of degrading the ECM by secreting proteases. Invadopodia grow and penetrate the ECM by extending the actin cytoskeleton, encouraged by the interaction of intracellular proteins [2]. The kinetics of their development is therefore influenced by the expression of these intracellular proteins, but also by the rigidity and density of the ECM, which favours its degradation [3]. The process of tumour invasion and the behaviour of these structures must therefore be addressed using both a biochemical and biomechanical approach, with biochemistry enabling the molecules involved to be identified and biomechanics enabling their mechanical impact to be quantified and analysed.

However, due to the lack of information at the cell-ECM interface, the biomechanical problem representing cell growth through the formation of invadopodia is poorly understood. For several years, various techniques for identifying multiphysical parameters have been developed, in particular to characterise the mechanical behaviour of materials and structures. Several identification strategies based on field measurements have been developed [4-8], but their application to experimental data is not always optimal. Potentially partial field measurements are generally subject to noise and the boundary conditions are often poorly known. Managing the boundary conditions is a challenge for identification methods, as the displacement and stress distribution are rarely known across the boundaries. A numerical approach based on an inverse method, the evanescent regularisation method [9-11], has been developed to identify boundary conditions from digital image correlation (DIC) field measurements. The stress distribution along the boundary where the load is applied is used to obtain an equivalent stiffness modulus for the material under study. The material parameters identified provide only a macroscopic response of the two-dimensional (2D) structure, since the linear behaviour law postulated is that of a homogeneous material.

Previous work:

Preliminary work has been carried out in our laboratory, in collaboration with the CoMeT biology laboratory at the University of Poitiers, involving the culture of human glioblastoma cells and the measurement of kinematic fields using digital volume correlation (DVC) from confocal microscopy volume images of glioblastoma cells [12]. Experiments at this scale of observation combined with measurements of kinematic quantities represent a major challenge for characterising the transformation of matter and interactions between cellular structures. It is also planned to carry out numerical modelling of the geometry using 3D image processing and segmentation techniques to predict the behaviour of structures on a cellular scale [13,14]. However, building a model that can be used by the finite element method requires a good knowledge of the boundary conditions.

We have developed a tool for reconstructing kinematic fields and identifying boundary conditions from 2D field measurements on a homogeneous material [10]. The inverse method developed is the evanescent regularisation method, and the method of fundamental solutions (MFS) [10] or the finite element method (FEM) are used to discretise the space of solutions of the equilibrium equation governing the elasticity problem. The inverse method has already been applied to 3D cases for acoustic problems governed by the Helmholtz equation [15].

We will extend the field of application of the evanescent regularisation method, which allows measured fields to be completed and boundary conditions to be identified from incomplete measurements, to cell biology.

Planned thesis work :

The aim of this thesis is to develop a new identification method based on an inverse method, which will make it possible to study the invadopodia formation process and quantify the mechanical fields required for their invasion into the ECM. The inverse method, using finite element modelling, will have to be implemented for volumetric cases in order to determine, from the cell and ECM displacement fields, the forces acting at the cell-ECM interface during invadopodia formation. In addition to the dimensional aspect, the extension of the method will take into account the heterogeneous anisotropic behaviour of the cell. This work will make it possible to calculate the internal forces at the cell-matrix interface from displacement field measurements (confocal microscopy and DVC) in gelatin, whose linear behaviour is known. The displacement fields of the cell will also be measured, and we will then know the displacements and stresses at the cell-matrix interface.

This body of work represents fundamental developments of the inverse evanescent regularisation method, with, from a numerical point of view, the extension of the method to the identification of interface conditions from kinematic fields and the recording of material parameters of a heterogeneous structure with finite element simulation, as well as the development of the identification procedure in 3D situations. From an experimental point of view, the method will be applied to volume data from DVC on a cellular scale. From a theoretical point of view, it will be possible to generalise the current tools to non-linear behaviours such as that of the cell. From the boundary conditions on part of the cell's plasma membrane, an inverse procedure for solving Cauchy-type problems could be used to calculate the boundary conditions in terms of displacements and forces on the entire cell envelope. This latter work would form an integral part of a major theoretical development for the evanescent regularisation method, which at present has always been applied to materials exhibiting linear behaviour [15,16].

Bibliography

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[16] Durand B., Numerical solution of Cauchy problems in linear elasticity in axisymmetric situations. International Journal of Solids and Structures, 2011.

MAIN SKILLS REQUIRED

Students with a Master's degree in mechanics or mathematics applied to mechanics will need to have acquired knowledge of mechanics and be comfortable with numerical programming.

FURTHER INFORMATION

COMPLEMENT	**Diploma required**: Master **Field of study** : Doctoral school registration at the University of Poitiers