Model developments for *in silico* studies of the lumbar spine biomechanics

Tesi Doctoral

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Chapter6

"Concern for humankind and the fate must always form the chief interest of all technical endeavours. Never forget this in the midst of your diagrams and equations"

(Albert Einstein)

Chapter6

MODEL DEVELOPMENTS FOR *IN SILICO* STUDIES OF THE LUMBAR SPINE BIOMECHANICS - GENERAL DISCUSSIONS & CONCLUSIONS -

A. Context & novelty of the study

I. Context

Since its development in the mid 20th Century, the finite element method has shown to be a reliable tool, not only in mechanical engineering, but also in other fields such as electronics, or thermodynamics. In biomechanics, the principles of continuum mechanics and constitutive equations so far successfully applied to plastics, metals, and rubbers, have demonstrated their potential to reproduce general behaviours of the musculo-skeletal system, when coupled to finite element models. The association of low back pain with mechanical factors has largely justified the development of lumbar spine models in an attempt to predict and explain mechanical dysfunctions due to alterations of the mechanical environment and/or spinal tissue components. Obviously, reliability of the predictions depends on model validations, as needed for any theoretical finding. Different types of mechanical measurements have been performed *in vivo* and *in vitro* on dissected spine specimens. Unfortunately, the *in vivo* mechanics of the musculo-skeletal mechanical system is still insufficiently determined to be truly modelled and serve for model validation. However, *in vitro* osteoligamentous spine systems could be more easily modelled and their general mechanical response could be reproduced *in silico*. Thus, many lumbar spine finite element models that were able to reproduce in vitro ranges of motion or intradiscal pressure measurements were used to assess the risk of low back pain in the healthy or pathologic spine. The outcomes of surgical treatments for low back pain are also being commonly investigated by means of finite element modelling.

Finite element predictions in spine biomechanics strongly pushed forward the transfer of knowledge and technology from theoretical mechanics to clinical reality. Nevertheless, some questions about the functional mechano-structural relations existing in living tissue remain unanswered. The fact that several lumbar spine models with differently detailed geometries and approximated mechanical laws were all able to reproduce *in vitro* experimental data, suggested that the validation methods used for these models were still incomplete. The mono- or multi-segment models, proposed for clinical assessment, were not investigated thoroughly enough to precisely identify limitations and focus on specific needs for the further improvement of the predictions. On the other hand, models presenting mechanistic descriptions of living tissues were generally too geometrically incomplete or had too many unknown parameters to be truly validated and demonstrate their value to face clinical problems.

II. Novelty

The present thesis is one of the first studies where internal lumbar spine biomechanics have been thoroughly investigated as a function of several parameters involved in the peculiarity of each model presented in the literature. The created L3-L5 bi-segment model included all the passive components of the osteoligamentous lumbar

spine. Level-dependent geometrical and mechanics characteristics were included and allowed assessing the interactions between different adjacent segments. Moreover, load transfers through the L3-L4, L4-L5 intervertebral discs and the whole L4 vertebrae could be assessed, as this region of interest was sufficiently far away from the imposed boundary conditions.

On one hand, the stepwise development of a geometrically accurate model, from a geometrically inaccurate model, allowed detailing the effect of ligament, vertebra, and intervertebral disc geometries on the load transfer between different components. As a new contribution to the field, it was found that although the global behaviour of both geometrical models could be successfully validated, internal biomechanics was still an undetermined system. Nevertheless, comparison of the predicted role of ligaments and intervertebral discs, with literature data, showed that the geometrically accurate model was most likely to give more truthful load transfers than the original inaccurate model. Based on such outcome, it was hypothesized that, even if the global behaviour of a spine segment can differ in geometry from one to another, the relative biomechanical role of the different components might remain constant. This constituted a solid basis to draw precise recommendations on how in vitro data and finite element modelling should be used together to increase the level of confidence of predicted internal load transfers.

On the other hand, the geometrically accurate model was used to study in detail the functional biomechanics of the intervertebral disc as a function of different possible annulus structures. It was shown that interactions between the nucleus pulposus and the annulus fibrosus, and between the intervertebral disc and the rest of spine models, highly depended on the annulus collagen fibre organisation. Different segment geometries may also affect these interactions. Due to the diversity of spine segmental geometries, this raised the new idea that intervertebral disc biomechanics should not be studied with any collagen fibre organisation taken from the literature, but with case-specific annulus anisotropies. Moreover, structure-loading local relationships were found to depend on the type of constitutive model chosen for the modelled tissues. As such relationships were shown to be important, it was concluded that phenomenological tissue models were insufficient to study the functional biomechanics of lumbar intervertebral disc and mechanistic constitutive models should be preferred. Such link between local and global biomechanics of the lumbar spine demonstrates the immediate need of mechanically improving lumbar spine intervertebral disc models, which had been rarely thoroughly discussed in the lumbar spine model literature.

In summary, the work performed in this study led to new important findings that allowed examining the limitations associated to the modelling techniques commonly used for lumbar spine finite element modelling. Such examination is very important as it led to identify the first priority developments necessary to improve the level of confidence of predicted internal biomechanics.

B. General discussions

I. Load transfers & lumbar spine components

In Chapter 1, a review of the lumbar spine functional anatomy was presented. In Chapter 2, the use of a L3-L4 lumbar spine bi-segment finite model, including most of the passive tissues of the normal spine, allowed identifying specific load transfers at a structural level. All modelled tissues were found to mechanically interact between each other, in a coordinated way that could be related to their *in vivo* structures and compositions. As such, Chapter 1 highlighted the biomechanical functionality of the lumbar, spine curvature, vertebral body sizes and shapes, zygapophysial joint shapes and orientations, and intervertebral disc structures and compositions. In turn, simulation results presented in Chapter 2 led to a better understanding of the functional tissue organization from the point of view of load distributions.

Tissues components such as the vertebral cortex or the intervertebral disc endplates do not directly contribute to the apparent biomechanical behaviour of the lumbar spine. Thus, their mechanical role is hardly accessible through common experiments, i.e. measurements of ranges of motion, instantaneous axes of rotation, intradiscal pressures, or disc bulging. Vertebral cortex and cartilage endplates are thus rarely a mater of discussion in biomechanical studies of the lumbar spine usually focused on intervertebral disc annuli and nuclei, ligaments, zygapophysial joints, and trabecular bone. However, results of Chapter 2 have showed that vertebral cortex and intervertebral disc endplates do significantly contribute to the load transfers between the nucleus, the annulus, and the trabecular bone.

Because high external loads are constantly acting on the spine, on one hand, intervertebral disc and trabecular bone mechanical responses are directly involved in the outcomes of pathologies such as disc degeneration or osteoporosis. On the other hand, according to the principles of mechanically-induced tissue (re)modelling (Roesler, 1987; Matyas *et al.*, 1995; Yamamoto *et al.*, 1996), the mechanical integrity and specific response of these spine components should not be considered without taking into account both the amount and the nature of the loads transferred by and to the surrounding tissues. A lumbar finite element model can be seen as a snap-shot of the corresponding real system, either in a healthy or in a pathological state, and might not require including any remodelling algorithm. Still, a model may be limited by its constitutive equations, if these are not able to reproduce the right nature of the loads locally generated in the tissues. Nevertheless, the conclusions drawn from Chapter 2, compared to the literature analysis of Chapter 1, showed that, as long as all passive tissues are included, basic tissue models are sufficiently good to further understand both the detailed biomechanics of the spine and the different model limitations.

II. Model developments & spine internal biomechanics

In Chapter 3, thanks to the geometrical update of the L3-L5 lumbar spine bi-segment model presented in Chapter 2, two different geometrical models were compared. Bone, intervertebral disc, and ligament geometries were found to have only little effect on the global apparent behaviour of the segments, under different load regimes. However, the internal load transfers and individual relative roles of the modelled components in resisting the simulated motions strongly depended on the geometrical peculiarities of each model. Thus, any particular model geometry needs to be calibrated to ensure predictions of realistic load transfers.

Model calibrations may involve specific adjustments of material properties and/or other approximated modelling parameter. As shown in Chapter 3, calibrations multiple experimental *in vitro* data on spine segments with successively removed components, e.g. ligaments, cartilages, etc…. should be used to quantify the relative action of each modelled spine component. Indeed, this kind of experimental data has been already used for a lumbar spine finite element model calibration, that mainly consisted in adjusting soft tissue material properties, until a large set of experimental ranges of motion could be reproduced (Schmidt *et al.*, 2007a). Nevertheless, results obtained in both Chapters 3 and 4, showed that focussing calibration studies on the reproduction of global behaviours may lead to non-unique predictions of the spine internal biomechanics, unless model geometries are fully characterized.

Soft tissues such as ligaments and intervertebral discs generally hinder complete geometrical characterizations of spine segments. Although rarely used, magnetic resonance imaging techniques could determine ligament outlines and intervertebral disc geometries. Nevertheless, these tissues are highly organized composite structures. They are known to be mainly composed of collagen and/or elastin fibres embedded in multiphasic ground substances (Chapter 1), but knowledge about the precise amount and organization of these fibres is still limited. Unfortunately, such compositional/geometrical parameters appear essential to truly describe the internal spine biomechanics, and should be investigated in parallel with soft tissue constitutive equations (Chapter 4).

Quantifying different fibre contents/organizations in soft tissues can be obtained through destructive biochemical assays and dissection techniques. Unlike X-rays, dissection techniques can lead to very precise results for the mapping of three-dimensional fibrous organizations, but are very demanding and time-consuming (Holzapfel *et al.*, 2005). Moreover, while destructive characterizations are only acceptable for the modelling of spine specimens taken out from cadavers. Results from Chapter 4 have shown that lumbar spine finite element models can be used as mathematical tools to investigate the fibrous organization of soft tissues, in particular model geometries. Nevertheless, this kind of study requires assuming particular biomechanical roles of the investigated tissues, and these roles need to be associated, to the optimization of predictable parameters.

In Chapter 4, the choice of these parameters was basically based on the assumptions that optimal tissue configurations generate mechanical conditions

respecting tissue integrity. Beside avoiding tissue overloading and mechanical breakage, the idea of tissue integrity is linked to the biological notions of metabolism and catabolism, embracing maintenance, remodelling, and repair of the extracellular matrices. It is now commonly accepted that specific mechanical environments can hinder or favour the synthesis of specific structural macromolecules, controlling both mechanical properties and biomechanical functionality of a tissue (Potier *et al.*, 2009). As discussed in Chapters 4 and 5, this phenomenon naturally leads to relate finite element model predictions with local mechanical environments, potentially influencing both cell activity and tissue functionality. However, such interaction between mechanics and biology involves a feed-back loop, in which cells affect their own mechanical environment by modifying the surrounding extra-cellular matrix and the way this matrix transfers external loadings. Thus, predicting optimal mechanical conditions respecting tissue integrity is still limited by the constitutive equations commonly chosen for lumbar spine finite element modelling. As such, as suggested in the concluding discussions of Chapter 4, sorting out how interstitial fluids influence local stress/strain tensors would already greatly improve the coherency between local soft tissue structures and biomechanics.

III.Lumbar spine models & clinical assessment

The advantage of being able to use lumbar spine models for clinical assessment is obvious. Medical imaging techniques are now sufficiently advanced so that patient-specific geometries of different motion segments can be modelled within reasonable timelines. These models can help understanding the mechanical outcomes of pre-existing deformities due to accidents, bad postures, abnormal genetic programming, etc…, and help clinicians to find appropriate solutions for pain or mobility troubles. Surgical solutions, involving sudden modifications of the spine structure, can be first evaluated *in silico*, by modelling the treated spine and compare it to the unmodified spine model, or additionally, to a virtually non-pathologic spine model of the patient. If any engineered materials or structures need to be implanted, modelling the implants and predicting their mechanical interactions with the lumbar spine model can help adjusting designs and taking into account possible biomechanical disturbances. Indeed, many finite element studies were reported to this respect and are already cited in Chapters 1 and 5. Unfortunately, all these studies suffer similar limitations as those highlighted in Section B.II. of this concluding Chapter.

Accordingly, authors are generally cautious with the interpretation of their simulation results and they mainly build qualitative conclusions that aim to guide the attention of clinicians and prosthesis designers on possible negative outcomes. Among 10 peer-reviewed works, covering a time period of 8 years, six highlighted limitations due to inaccurate boundary conditions (Chen-Sheng Chen *et al.*, 2001; Goel *et al.*, 2005; Zander *et al.*, 2002; Chen *et al.*, 2008; Noailly *et al.*, 2005; Moumene and Geisler, 2007), five pointed out limitations due to idealizations of post-surgery configurations (Zander *et al.*, 2002; Dooris *et al.*, 2001; Lacroix *et al.*, 2006; Chen-Sheng Chen *et al.*, 2001; Noailly *et al.*, 2005), three mentioned limited predictive power due to tissues modelled as linear isotropic materials (Zander *et al.*, 2002; Chen *et al.*, 2008; Polikeit *et*

al., 2003a), and two related at least one of the limitations to geometrical approximations (Dooris *et al.*, 2001; Polikeit *et al.*, 2004). Nevertheless, in the treated lumbar spine models, neither the influences of these limitations on the predicted load transfers, nor their consequences on the discussed results, were thoroughly investigated. In two studies, it was even stated that identified limitations should not affect the trends pointed out by the reported computational investigations (Goel *et al.*, 2005; Zander *et al.*, 2002). Results presented in Chapters 3 and 5 illustrate the risk that such statement represents.

First of all, different lumbar spine model geometries may lead to different load transfers through individual modelled components (Section B, Chap 3). For *in silico* evaluation of any implant or any anatomical reduction, intact lumbar spine finite element models are locally modified to model new post-surgical configurations. Comparison of the intact and treated models will then quantitatively and qualitatively depend on the particular role of the replaced or removed component in transferring loads to other components. Therefore, if load transfers are geometry-dependent, the evaluation of any surgical procedure by means of finite element modelling will also depend on the particular geometry of the initial model. Unfortunately, at such point, nothing allows claiming that trends observed with one model geometry will be similar in other geometries. The creation of patient-specific model geometries would solve great part of the problem.

In Chapter 5, the type of boundary condition, i.e. load- or displacement-controlled rotations, and rotations with or without compressive follower force, largely affected the distribution of the internal forces among the different components. For some modelled tissues, this resulted either in overloading or load relieve. It was, however, suggested that some load cases, such as displacement-controlled rotations with follower compressive force, might be more representative of the lumbar spine *in vivo* loading than other load cases, such as simple load-controlled rotations. Moreover, as discussed in Chapter 5, other reported loading methods were showed to be potentially even more accurate (Goel *et al.*, 2005; Panjabi, 2007). However, none of these uniform loadings takes into account muscle forces. Stress distributions reported for the lumbar intervertebral discs of a lumbar spine model, coupled to a model of back muscle network (Zander *et al.*, 2001), suggests that the varying distribution of muscle-induced forces along the lumbar spine ((Bogduk *et al.*, 1992), Chap1) might significantly diverge from uniform external loadings. Thus, if basic boundary condition changes (as modelled in Chapter 5) already affected the predictions of prosthesis effects on the lumbar spine model biomechanics, it seems difficult to gauge the likely influence of real *in vivo* forces, even qualitatively. Regrettably, local muscle actions in multi-segment lumbar spine samples are still insufficiently known to be modelled with reasonable levels of confidence. Simplified uniform loads, as used for *in vitro* testing, are then still preferred.

Independently of the boundary conditions, predictions of adjacent level effects, performed by comparison between a treated and an intact model, also depend on the veracity of the calculated load transfers. For example, considering adjacent intervertebral discs, among other limitations, phenomenological models discussed in Chapter 4 only allow drawing very qualitative and general assumptions. Mechanistic models would allow more local mechano-biological evaluations of any studied

treatment, and such local analyses may help to overcome some problematic points linked to undetermined boundary conditions. Given the current state of knowledge of spine biomechanics and the current development of the models, reliability of lumbar spine clinical assessment by means of finite element modelling seems to be limited to the evaluation of ranges of motion. However, discussions from Chapter 5 showed that this kind of evaluation already allows assessing the potential of a new treatment in restoring segmental mobility, and help predicting the displacement fields that an implanted device may feel. Such information is valuable to guide the first steps of solution design for low back pain. But the real potential of finite element modelling, i.e. accessing data that experiments cannot give, and anticipate long-term clinical outcomes cannot be exploited yet. Additional clinical, experimental, and theoretical knowledge is still required. Provided that these three fields of knowledge can merge in a coordinated manner to further develop spine modelling techniques, accelerated improvements in low back pain treatments are ensured.

C. General conclusions

In this thesis, six new osteoligamentous lumbar spine bi-segment finite element models were created:

- One based on inaccurate geometries of vertebrae, ligaments, and intervertebral discs
- One based on accurate geometries of the different modelled components
- Four based on accurate geometries, poroelastic nuclei pulposi and four different fibre-induced anisotropy of the annulus fibrosus

All together, these models showed that reliable use of lumbar spine finite element models to complement both clinical and *in vitro* data requires precise descriptions of local tissue loading and response. Nevertheless, results also showed that local predictions of load transfers between

- Ligaments, intervertebral disc, and zygapophysial joints
- Intervertebral disc and vertebral body
- Nucleus pulposus and annulus fibrosus

are usually quantitatively and qualitatively limited by factors such as:

1. Soft tissue structural organisation
2. Tissue material properties
3. Boundary conditions

From the different discussions, it came out that points 1. and 3. would *a priori,* necessitate further knowledge in anatomy and kinematics from the fields of clinical and experimental biomechanics. However, such knowledge cannot be immediately acquired and, in the meantime, lumbar finite element models can contribute and serve as *in silico* laboratories for there own development. As such, it was shown that, for any peculiar lumbar spine geometry, point 1. could be numerically assessed through an optimization

procedure, involving both theoretical and experimental inputs. However, point 2. needs to be previously studied.

These findings allow then proposing a hierarchical procedure for the first development of qualitatively reliable finite element models:

a. Acquisition of a precise and consistent overall geometry (medical imaging, morphological measurements, etc…).
b. Implementation of mechanistic models for the soft tissues, especially the intervertebral disc. Composition and structure-related fluid effects have to be incorporated (osmolarity, porosity).
c. Statistical quantification of the constitutive equation parameters with mechanical testing of isolated tissues.
d. Numerical analysis of the quantitative functional organization of the soft tissues modelled within a particular lumbar spine model geometry. Statistical *in vitro* data on different complete and anatomically reduced segments should be used.
e. Use of statistical *in vitro* data on different complete and anatomically reduced segments to verify the relative role of the individual components included in the lumbar spine model. Adjustment of constitutive equation parameter values if necessary.

Following these model development steps, consistent local load transfers could be studied under different types of boundary conditions. Then, for a specific study, approximated boundary conditions could be considered as limitation or not, depending on their influence on local regions of interest. Furthermore, a lumbar spine finite element model, created as proposed above would fill the minimum requirements to start coupling mechano-biology theories and go even deeper into the understanding of the normal spine.

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"Social living is the best."

(Burning Spear)

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Ein grosser Teil meiner Kentnisse über Wirbelsäulenbiomechanik kommt aus Ulm, wo ich während meiner Doktorarbeit die Gelegenheit gehabt habe, drei Monaten am Institut für Unfallchirurgische Forschung und Biomechanik mit Profesor Wilke zu arbeiten. Dort habe ich nicht nur viele Erfahrunmgen gewonnen, sondern auch Freundschaften. Dafür würde ich mich gerne bei Achim, Connie, Annette, Frank und speziell bei Hendrik und Oli herzlich bedanken.

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Beyond my PhD work, I also had the chance to closely collaborate with persons from other institutions who indirectly greatly supported my efforts through their friendship and knowledge. Among these persons, I would like to thank particularly Esther, David, Manu, Frederico, and Keita. Guys, you did not only gave me the emotional strength I was needing to finish this book, but our discussions and work together in different scientific areas did significantly improve the quality of the report. Thank you so much for this.

Ciències, art, bogeries, riures, somnis, projectes, i amistat. Durant aquests últims anys, tot això ha representat una part important de l'energia que m'ha permès sobreviure a la tesi doctoral i mantenir la il·lusió, inclòs en els moments de dubtes. Així doncs, m'agradaria donar les gracies a uns grans amics que contínuament m'han anat alimentant de valor amb totes les seves particularitats i diversitats com a persones. Biel, Delfi, Martita, Jordi, Ferran, Adri, Fran, Oscar, Gaëtan, Lucile, Santi, Adriana, GRÀCIES, MOLTISSÍMES GRÀCIES per haver estat aquí!

Finalmente, usaré el idioma con el cual nos conocimos para agradecer con todo mi corazón a Soraya, compañera de todos los instantes desde el principio del doctorado. Sorah, este libro te está dedicado, pero creo que nada puede expresar realmente el amor que ha acompañado los pasos de esta tesis y ha contribuido a su finalización. Es una gran suerte y un gran honor para mí haber tenido el privilegio de tal apoyo.

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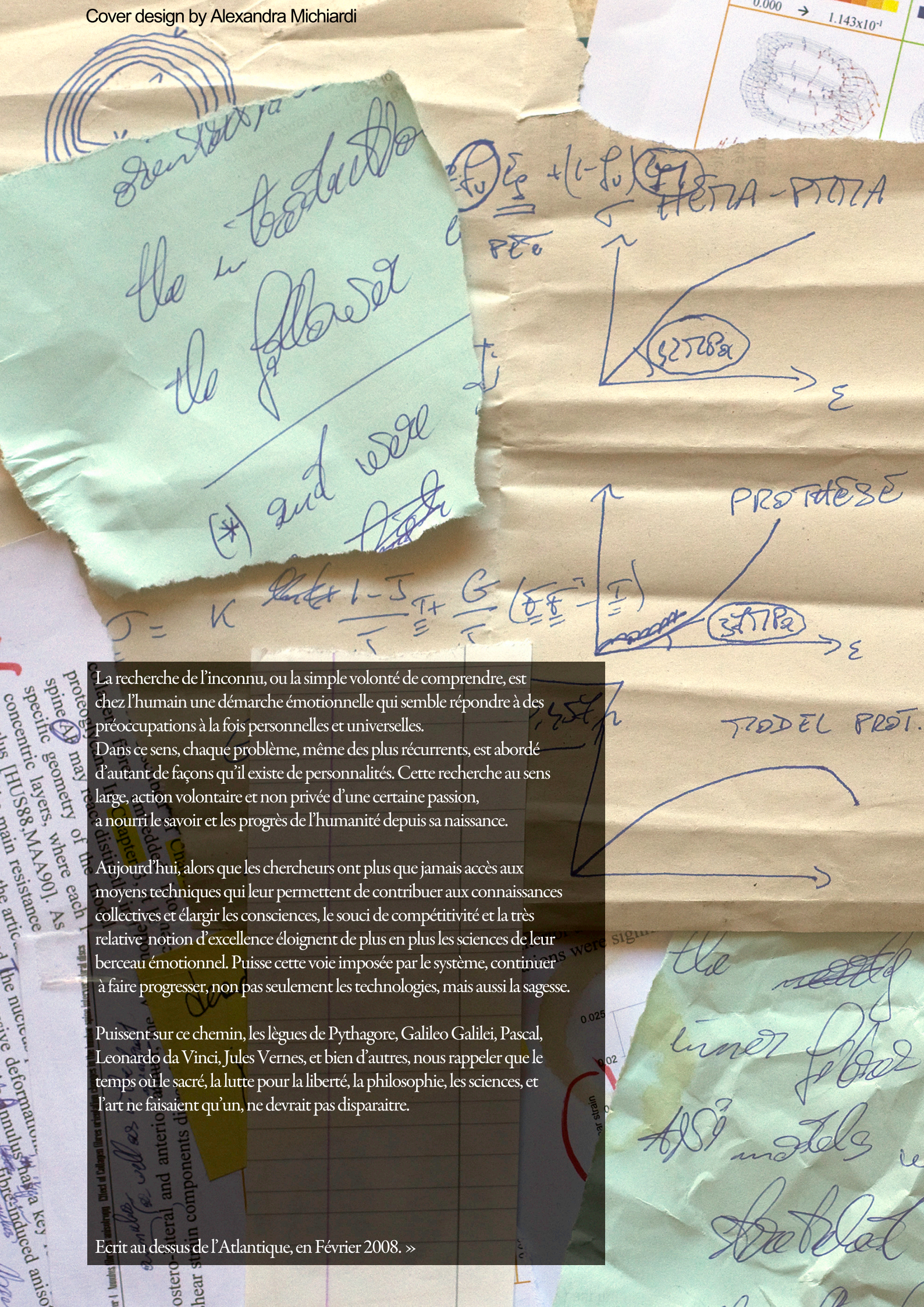

La recherche de l'inconnu, ou la simple volonté de comprendre, est chez l'humain une démarche émotionnelle qui semble répondre à des préoccupations à la fois personnelles et universelles.
Dans ce sens, chaque problème, même des plus récurrents, est abordé d'autant de façons qu'il existe de personnalités. Cette recherche au sens large, action volontaire et non privée d'une certaine passion, a nourri le savoir et les progrès de l'humanité depuis sa naissance.

Aujourd'hui, alors que les chercheurs ont plus que jamais accès aux moyens techniques qui leur permettent de contribuer aux connaissances collectives et élargir les consciences, le souci de compétitivité et la très relative notion d'excellence éloignent de plus en plus les sciences de leur berceau émotionnel. Puisse cette voie imposée par le système, continuer à faire progresser, non pas seulement les technologies, mais aussi la sagesse.

Puissent sur ce chemin, les lègues de Pythagore, Galileo Galilei, Pascal, Leonardo da Vinci, Jules Vernes, et bien d'autres, nous rappeler que le temps où le sacré, la lutte pour la liberté, la philosophie, les sciences, et l'art ne faisaient qu'un, ne devrait pas disparaitre.

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