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Biomechanics of Living Organs: Hyperelastic Constitutive Laws for Finite Element Modeling

Chapter 22: Spine

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Abstract

Clinical problems of the human spine have a high prevalence, affecting more than 25.5 M persons 2012. Older adults, in particular, form a continuously growing age group, with degenerative spine disorders such as deformities or osteoporosis. A basic requirement for proper management of various spinal disorders, effective injury prevention and rehabilitation is a detailed knowledge of the fundamental biomechanics of the spine. Despite the growing interest for biomechanical research on the spine during the last decades however, many clinical problems remain largely unsolved due to the poor understanding of the underlying degeneration phenomena and the complexity of the spinal construct. In particular, diagnosis is challenging, because of the lack of tools to quantitatively assess soft tissue alteration and because the most relevant clinical indices for diagnosis are not clearly established. Driven by the ever-growing computer power and imaging devices, the development of FE models has become widespread and have allowed to overcome some of the existing shortcomings (invasiveness, complexity of the organization of the biological tissues and complexity of establishing the loads present in the human spine). These have thus emerged as powerful and reliable tools with considerable applications in surgery planning, in studying the etiology, progression and effects of spinal deformities and intervertebral disc. These models have enhanced our understanding of the spine and will continue to do so in the future. In our group, numerical work performed using of a FE modeling has highlighted the paramount influence of both geometric patient-specific modeling and *in-vivo* personalization of tissue mechanical properties. There are many exciting avenues for future research. Amongst these, the question of the validation of computational modeling and simulation with the perspective of supporting the development of medical devices is central.

Keywords: Spine, Finite Element Modeling, patient-specific modeling, in-vivo personalization of tissue mechanical properties, multi-scale modeling

1. Introduction

Spine disorders affect a large portion of the population, from children and adolescents (who suffer from deformities or trauma), to working age adults. 25.5 M persons were affected in 2012 by back or neck pain, resulting in 290.8 million workdays lost (Lezin and Watkins-Castillo, 2016). Older adults form a continuously growing age group, with degenerative spine disorders such as deformities or osteoporosis, which affects 10 M Americans, mostly women.

Prevention is a key factor. However, it is still difficult due to the poor understanding of the underlying degeneration phenomena and the complexity of the spinal construct. Moreover, diagnosis is challenging, because of the lack of tools to quantitatively assess soft tissue alteration and because the most relevant clinical indices for diagnosis are not clearly established. A subject-specific basis for treatment strategy is limited, since the cause of spinal disorders is often multifactorial. Although surgery is widely used, the rate of mechanical complications is still high, particularly for spinal deformities (Ha et al., 2013). Such complications are often unpredictable because the mechanisms yielding mechanical complications are difficult to understand. In this context, a biomechanical analysis of the spine is essential to better understand physiological behavior, the injury mechanisms and the key factors to take into account in treatment.

Built on the pelvis, which is articulated at the two hips, and ending by the head (which weighs on average 40 to 55 N (Vital and Senegas, 1986)), the spine is a composite assembly constituted of relatively rigid complex shaped structures, the vertebrae, connected by articular facets and passive viscoelastic soft tissues, namely intervertebral discs and ligaments. Such a slender beam has a low intrinsic stability. Vertebrae and surrounding bone structures are interconnected by a complex set of active muscles driven by the neuro-control system ensuring the spine function. From a biomechanical point of view, the spine has 3 main functions: (i) maintain the erect position and establish a stable motion while (ii) supporting resulting static and dynamic loads and (iii) protecting the brain and spinal cord. This last, but not least function requires shock absorption (so that heel strike impact, for example, does not induce vibrations in the brain) and strict control of intervertebral motion to prevent spinal cord or nerve damage.

The basic component of the spine structure, the Spinal Functional Unit (SFU), consisting of two vertebrae and the adhering soft tissues, has to ensure the above described mechanical functions. A strongly non-linear behavior, i.e. low stiffness motion at physiological ranges and high stiffness at sup-physiological ranges, is necessary to limit abnormal motion that can be extremely dangerous for the medulla and nerve roots. Viscoelastic behavior is also essential to ensure shock absorption. While the global SFU arrangement is similar all along the spine, strong differences exist among the cervical, thoracic and lumbar vertebral levels.

In a gross description, vertebrae from C2 (second cervical vertebra from head) to L5 (lowest lumbar vertebra) are composed of a vertebral body and a posterior arch, connected by pedicles. The posterior part on the vertebral body, the pedicles and laminae delimitate the space for the medullar canal. In addition, the posterior arch includes spinous and transverse processes with insertion zones for ligaments and muscles, and a bone mass supporting articular facets which shape and orientation vary along the spine, as shown in figure 1.

These vertebrae are connected by the intervertebral disc and a series of ligaments, of different shapes and functions. The intervertebral disc is a composite structure based on a ground matrix, rich in proteoglycans, with a peripheral structure of embedded fibrous lamellae, called the annulus fibrosus. The central part,

the nucleus pulposus, is highly hydrated and can be assimilated to a fluid. At the microstructural level, the annulus fibrosus comprises concentric layers of alternately crisscrossed collagen fibers, with possible discontinuities of some layers (Marchand and Ahmed, 1990). Annular layers are connected by an inter-lamellar elastin network (Smith et al., 2008). This interface plays an important role in the global mechanical response of the intervertebral disc (Adam et al., 2015).

The ligaments, uniaxial fibrous structures with a highly nonlinear behavior due to the arrangement of their consisting collagenous fibers, are highly deformable at physiologic ranges of motion and turn very stiff when a threshold is reached. Because of their mechanoreceptors, they are mainly considered as stabilizers and sensors at the source of co-contraction which is necessary for refined and controlled motion (Solomonow, 2006).

Longitudinal anterior and posterior ligaments run vertically all along the spine with connections to vertebral bodies and discs for the anterior ligament and to the vertebral bodies alone for the posterior one. *Ligamenta flava* (or yellow ligaments) ensure the posterior covering of the medullar canal. They connect the laminae of adjacent vertebrae and fuse with the facet joints capsules. The intertransverse and interspinous ligaments connect the transverse and spinous processes respectively. The supraspinous ligaments connect the apexes of the spinous processes (from C7 to sacrum). The capsular ligaments surround the facet joints.

2. Vertebral mobility

The Spinal Functional Unit (SFU) is the basic building block of the spine, consisting of two adjacent vertebrae, the intervertebral disc, the facet joints, and the spinal ligaments. Analysis of the mechanical and kinematic responses as well as the load distribution within the SFU joints, under the application of an external load, is paramount for understanding the spine and its various pathologies. The following presents an overview of the most important biomechanical aspects of the functional spine unit.

Loads on the spine and posture

One of the functions of the spine is to support the bodyweight and to maintain the body in the upright position. In this configuration, the subject is never entirely immobile: the body constantly effectuates micro-movements to ensure equilibrium.

In the upright position, each functional spine unit experiences the weight of the body segment superior to it. Concerning the maximal admissible loads at the level of the intervertebral joint, literature contains little information. Generally, these are measured via *in-vitro* quasi-static or dynamic experiments in which the functional spine unit is loaded until failure. The maximum admissible loads vary from 1000 N – 4000 N for the cervical spine to 5000 N – 13000 N for the lumbar spine (Hutton and Adams, 1982; Nuckley et al., 2013; Panjabi and Myers, 1995; Skalli et al., 2007). Note however that, although the physiological charges are rather high (100 N – 400 N for the cervical spine and 3000 N – 5000 N for the lumbar spine) (Nachemson, 1975; Wilke et al., 1999; Yoganandan et al., 1991), the torques low: 2 Nm for the cervical spine up to 20 Nm for the lumbar spine. Hence, a slight postural deviation might yield an eccentric load which gives rise to torques exceeding the threshold. Consider for example a section at the level of the L3-vertebra. At this level, the gravity force direction vector passes through the center of the vertebral body. Hence, there is no need for important muscle forces to ensure equilibrium. The weight of the body segment superior to L3 is estimated at 400 N. Hence, the compressive forces sensed by L3 respect the physiological load threshold. However, when the load eccentricity is augmented by for instance 5 cm due to postural changes, the body weight induces a moment of 20 Nm, the load limit. Moreover, considerable muscle activity is required to counterbalance this moment, thus increasing the compressive forces on L3. This illustrates the importance of postural analysis.

Range of motion under external loading

At the level of the functional spine unit, the spine has six degrees of freedom (DOF): three rotational and three translational DOF. The movement amplitudes, i.e. the ranges of motion (ROM), are limited by osseous abutments, the intervertebral discs and the ligaments. Antero-posterior shear is limited by the facet joints and by the disc, whereas stability in flexion is ensured by the facet joints, by the anterior edges of the vertebral body and by the posterior ligaments. The amplitude of the extension movement on the other hand, is determined by the contact between the spinous processes, the posterior edges of the vertebral bodies, the facet joints and by the anterior ligaments. Under lateral bending and axial rotation, the osseous abutments are the unciniate processes (only in the cervical spine) and the facet joints (Barrey, 2011).

Due to the orientation and the architecture of the articular surfaces, the six DOF's are not entirely independent from one another: lateral bending is very often coupled to ipsilateral rotation and vice versa. Movement coupling between lateral bending and axial rotation is most significant in the cervical spine (Clausen et al., 1997; Maurel et al., 1997).

The description of the functional spine unit mobility remains a scientific venture. The large variability in the literature data relates to this. Literature proposes *in-vitro* analysis techniques and direct *in-vivo* measurements to record both the principal and coupled motion and to extract the ROM. The classic *in-vitro* analysis involves the blocking of all DOF's of the inferior vertebra and the exertion of a pure moment onto the superior vertebra in the three different directions, resulting in a flexion-extension, a lateral inclination or an axial rotation (see also Figure 2). As such, the rotational kinematic response can be extracted (Lavaste, 1997; Lima, 2014). However, literature contains few records of comparable *in-vitro* analyses for the estimation of the translational kinematic response under the application of a pure force, especially for the cervical and thoracic spine (Oxland, 2016).

The typical load-displacement behavior of a functional spine unit in flexion-extension is depicted in Figure 3 for the cervical spine and in Figure 4 for the lumbar spine. The highly non-linear curve is characterized by a hysteresis, which is due to the viscoelastic behavior of the complex and the elastic energy dissipation during load discharge (Lima, 2014). Note also the presence of a so-called 'neutral zone'. It is the zone of physiological displacement of the upper with respect to the lower vertebra, in which large movement is possible without significant resistance (Panjabi, 1992). The neutral zone covers a significant part of the ROM in the cervical spine but is almost absent in the lumbar and thoracic spine. For the cervical spine the neutral zone represents on average as much as 50% of the ROM. The most important neutral zone is obtained at the C1-C2 unit, where it can reach 80% of the movement amplitude (Panjabi, 1992; Wen et al., 1993; Wilke et al., 1994; Yamamoto et al., 1989). However, for both the thoracic and the lumbar spine, the neutral zone spans at the most 2% of the ROM.

Figure 5 visualizes the repartition of the ROM for each spine segment among the constituting functional spine units, based on literature data (Watier, 1997; Yamamoto et al., 1989; Yaszemski et al., 1992) and data collected at the Institut de Biomécanique Humaine Georges Charpak. The following describes the mobility of the functional spine unit for each spine segment individually.

1) The cervical spine:

Table 1 lists the rotational ROM in the three anatomical planes for each cervical functional spine unit. Figure 11 illustrated the relative contribution of the cervical spine in the mobility of the spine.

The flexion-extension of the C0-C2 segment represents about 35% of the total ROM. The same segment is responsible for about 35% of the mobility in lateral bending. Concerning axial rotation, a highly significant increase from C0-C1 to C1-C2 can be noted. The axial rotation of the C0-C1 functional spine unit corresponds to about 9% of the total movement amplitude, as is the case for the functional spine units in the C2-C7 segment. However, 50% of the total axial rotation is achieved in the C1-C2 functional spine unit alone.

The most important mobility is obtained in flexion/extension. The cervical spine is somewhat less mobile in lateral bending. Apart from the significant axial rotation in the C1-C2 unit, this mobility is also rather limited.

Table 1: The ROM for the cervical functional spine unit (based on (Watier, 1997), the standard deviation is approximately 5° per functional spine unit)

Flexion/Extension	Lateral Bending	Axial Rotation
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C0-C1	24°	10°	7°
C1-C2	18°	16°	71°
C2-C3	11°	9°	9°
C3-C4	15°	10°	10°
C4-C5	17°	9°	9°
C5-C6	19°	9°	8°
C6-C7	16°	9°	6°

Contrary to the thoracic and the lumbar functional spine units, the cervical functional spine unit contains the uncovertebral joint defined as the articulation between the uncinat processes on the superior plateau of the inferior vertebra and the vertebral body of the vertebra above. This explains the increased importance of coupled motion in the cervical spine with respect to the rest of the spine. Under lateral bending, the associated axial rotation reaches on average 25% to 60% of the principal movement, except for the C1-C2 functional spine unit, in which the coupling ratio can be as high as 220%. Under axial rotation however, the coupled bending movement spans 25% to 80% of the principal movement. A superior coupling ratio of 110% can be measured in the C2-C4 segment.

2) The thoracic spine:

Table 2 summarizes the rotational ROM in the three anatomical planes for each thoracic functional spine unit. Figure 11 illustrated the relative contribution of the thoracic spine in the mobility of the spine.

It is interesting to note that the intervertebral mobility in flexion/extension of the inferior part is higher than for the superior part of the thoracic spine. However, in lateral bending, the functional spine unit mobility stays rather constant. The maximal measured difference between the different units is about 2°. Considering axial rotation, the intervertebral mobility remains constant for the functional spine units between T1 and T8, below which a decreased mobility is observed.

Table 2: The ROM for the thoracic functional spine unit (based on (Yaszemski et al., 1992))

	Flexion/Extension	Lateral Bending	Axial Rotation
T1-T2 to T3-T4	4°	6°	8°
T4-T5 to T7-T8	6°	8°	8°
T8-T9 to T11-T12	12°	8°	4°

3) The lumbar spine:

Table 3 collects for each functional unit of the lumbar spine, its rotational ROM in the three anatomical planes. Figure 11 illustrated the relative contribution of the lumbar spine in the mobility of the spine.

As for the thoracic spine in flexion/extension, the intervertebral mobility evolves progressively from L1-L2 to L5-S1. As a consequence, most of the total flexion/extension mobility of the lumbar spine is achieved in the L4-L5 and L5-S1 segments, i.e. 50% of the total ROM. However, in lateral bending, the growing mobility reaches a plateau at the L4-L5 unit. Regarding axial rotation, it has been shown that the intervertebral mobility increases from L1-L2 to reach a maximum at L3-L4. Then, a steady decrease with around 1° per functional spine unit is noticed.

The most significant amplitudes are obtained at the L4-L5 and L5-S1 functional spine units under flexion/extension. The amplitudes for axial rotation are very low, compared to those for flexion/extension and lateral bending. The difference can be as high as a factor 6.

Table 3: The ROM for the lumbar functional spine unit (based on internal data of the *Institut de Biomécanique Humaine Georges Charpak* and (Yamamoto et al., 1989), the standard deviation is approximately 3° per functional spine unit)

	Flexion/Extension	Lateral Bending	Axial Rotation
L1-L2	10°	10°	4°
L2-L3	11°	14°	5°
L3-L4	11°	11°	5°
L4-L5	14°	11°	4°
L5-S1	18°	11°	3°

Finite Element Analysis (FEA) has turned out to be a useful tool to investigate the implications of the vertebra morphology on the mobility of the spine. Through the use of a Finite Element (FE) model based on cadaveric spine samples, (Clausen et al., 1997) and (Maurel et al., 1997) indicated that the uncovertebral joints and the orientation of the facet joints are the main contributors for movement coupling in the cervical spine. (Laville et al., 2009) showed, with 16 subject specific FE models similar to the one described by (Maurel et al., 1997), that geometric inter-subject variability explains a major part of the motion variability at least in lateral bending and axial rotation. However, for flexion and extension movements, such a correlation was not found. The authors therefore ascribed the weak correspondence to the material behavior, which was not personalized. Hence, a detailed description of the material properties of the different elements of the spine seems necessary to fully explain its motion.

3. Intervertebral disc

Human beings have a very specific neuro-musculo-skeletal structure linked to their bipedalism. Behind this uniqueness in the animal world is hiding a richness and a remarkable biomechanical complexity that allow the spine to achieve key features such as support the body weight, move into space with a very large range of motion or damp shocks propagation coming from the lower limbs to protect the brain. Some of these key features might seem at first glance paradoxical: stability and movement, stiffness and flexibility, dissipation and economic movement. Thankfully, the spine is equipped of a very original and remarkable biomechanical component: the intervertebral disc (IVD).

The IVD is a unique soft tissue which provides fundamental features to the spine: support, flexibility and damping. These features, and more globally the overall mechanical response of the spinal joints, are directly linked to the disc tissue microstructure. One key feature of the IVD is its ability to sustain very large compressive loads while allowing mobility. From an anatomical point of view, the IVD is composed of two main structures: the annulus fibrosus (AF) and the nucleus pulposus (NP). The AF is a peripheral structure made of 15-25 orientated concentric lamellae (Marchand and Ahmed, 1990). These layers contain alternately angled collagen fibers (type I) embedded in a soft ground-matrix (Urban and Roberts, 2003). About 40% of the layers are discontinuous and the number of layers is generally lower in the posterior part of the AF and greater on the lateral sides. The outer layers are thicker (around 0.2mm) than the inner layers (around 0.14 mm) and the water content of the AF ranges from 78% at birth to 70% at end of life with mean value of 73% for an adult (Gu et al., 1999). The NP has a hydrophilic gelatinous core. Its matrix is made of collagen fibers organized randomly (80% of type II and 15% of type VI) and elastin fibers (Yu et al., 2002) that have a more radial arrangement. The proteoglycans (Johnstone and Bayliss, 1995) that represent 50% of the dry weight of the NP play a major role in the mechanical behavior of the disc by maintaining tissue hydration: the water content of the NP ranges from 90% at birth to 70% at end of life with mean value of 80% for an adult. From a biomechanical point of view, axial loads acting on spine leads to an increased pressure in the IVD. As the NP can be considered incompressible, the AF bulges outwardly, leading to an increased circumferential stress in the AF and an increased interlamellar shear stress. These internal forces balance the increased pressure in the NP.

The IVD is a very subtle component and can then be subjected to malfunctions which raise major challenges for the clinicians. The disc degeneration in young patients or due to aging can generate a biomechanical cascade associated with acute back pain. It is therefore very important to understand the operation and degeneration mechanisms that depend on the multiscale nature of the IVD.

a) Multi-scale modeling

A lot of authors have studied the anatomy of the IVD and its link with mechanical properties (Marchand and Ahmed, 1990; Markolf and Morris, 1974; Terti et al., 1991; Vergroesen et al., 2015) but little is known on the deformation mechanisms of this multi-layered structure. In particular, the role of the translamellar elastin fibers network radially linking the *annulus lamellae* at dedicated points could be of great interest (Urban and Roberts, 2003).

A recent study (Schollum et al., 2009) has been able to highlight in segments of the annular wall sectioned at a range of angles (oblique, in-plane, sagittal and transverse), the fibrous details of the translamellar bridging structures using differential interference contrast microscopy (DICM). This study has been able to quantify the number of bridges (about 12 in a 30 μm -thick oblique slice) and then to demonstrate that they were a significant anatomic structure that could be expected to play a significant biomechanical role.

A new study (Adam et al., 2015) has used polarized light micrography in a transverse cross-section to develop an image-based FE model incorporating sliding and separation between layers of the annulus (figures 6, 7 and 8).

In the transverse cross-section, the lamellar origin or termination or discontinuities were manually identified and used to generate a simplified micro/macro-scale FE model to study the effects of inter-lamellar interface mechanics and lamellar discontinuity on disc compression resistance. The mean thicknesses of the outer, middle and inner third of the lamellar layers in the disc cross-section at mid-height were used to define the corresponding lamellar thicknesses in the FE model.

This first disc FE model to incorporate interlamellar sliding and separation shows that disc compressive stiffness is relatively sensitive to interlamellar shear resistance, but not sensitive to interlamellar cohesion. With no other changes in geometry of material properties, allowing adjacent lamellae to slide freely across each other, reduces disc stiffness by 40% compared to the case where interlamellar interfaces are prevented from slipping.

Even if we are at the beginning of our understanding process, there is now strong assumption that inter-lamellar shear resistance could have a significant influence on the compressive stiffness of the IVD. Decreases in inter-lamellar shear resistance that could be linked to degradation of bridging collagenous or elastic fiber structures, might therefore be an important part of the process of disc degeneration.

b) Non-invasive biomechanical characterization

At a macroscopic level, if patient-specific modelling is gaining more attention because of its potential role in improving diagnosis and optimizing treatments, *in-vivo* personalization of tissues mechanical properties, although paramount, remains a major challenge. Currently, material properties are assessed using either *in-vitro* mechanical testing - currently the gold standard to determine IVD material properties - or inverse schemes based on FE models (Schmidt et al., 2013). These *in-vitro* experiments have enhanced our understanding of the IVD and will continue to do so in the future.

Ultrasound elastography is a non-invasive technique which has recently gained a lot of interest. It allows the evaluation of the tissue elastic modulus through the measurement of Shear Wave Speed (SWS) within the tissue (Tanter et al., 2008). Although ultrasound elastography has been a subject of research since the early 90s (Ophir et al., 1991), quantitative real-time techniques have only recently been introduced in the clinical setting (Tanter et al., 2008). Since then it has been successfully applied to assess several tissues, such as muscles (Gennisson et al., 2010), breasts (Athanasίου et al., 2010; Tanter et al., 2008) and liver (Bavu et al., 2011; Ferraioli et al., 2012), while preliminary work is being performed on several other soft tissues (Arda et al., 2011; Gennisson et al., 2010, 2011). In particular, until recently, the ability of SWS measurements to convey information on the tissue mechanical properties of the IVD had never been explored, partly due to the disc's relatively small size (with respect to shear wave wavelength), its non-homogeneous and anisotropic nature but also because of its position (sandwiched between two vertebral bodies, which could cause artefacts due to wave interference or mode conversion).

(Vergari et al., 2014a) first successfully explored the feasibility of intervertebral disc mechanical characterization by ultrasound elastography *in-vitro* in a bovine model. The authors reported a repeatability of 7% and a correlation was observed between Shear Wave Speed measurement in the IVD transverse plane and the functional unit compressional behaviour (figure 9), showing that this technique

has both a potential mechanical interest for the development of mechanical models but also a clinical interest for studying the etiology, progression and effects of spinal deformities and intervertebral disc (IVD) degeneration.

The authors also explored, for the first time, the feasibility of *in-vivo* quantitative assessment of mechanical properties of cervical discs (Vergari et al., 2014b) and reported reference values for asymptomatic subjects (n=47). The authors showed that shear wave elastography measurements were highly repeatable, not operator-dependent, and relatively easy to perform. Similar results were also reported for the biomechanical characterization of the lumbar annulus fibrosus in healthy children (n=31) (Vergari et al., 2016).

In-vivo non-invasive biomechanical characterization of intervertebral discs by shear wave ultrasound elastography represent a novel non-invasive biomarker for a range of spinal pathologies. This technique however yet remains to be compared to other means of assessment methods such as elastography measurements by Magnetic Resonance Imaging. Also, given the structure and function of the disc, analysis of the quasi-static behaviour alone is not sufficient for understanding normal disc function and assessing injury and damage mechanisms.

c) Viscoelastic Properties of the Intervertebral Disc (IVD)

Structure of the IVD and Viscoelasticity

The quantity of fluid inside the IVD is not constant but depends on the applied external load; if this is higher than the maximal acceptable pressure in the nucleus, the fluid is exuded, thus increasing the concentration of proteoglycans, and the nuclear pressure. The fluid flow continues until an osmotic balance is obtained; this corresponds to the equilibrium with the external load. Under a prolonged compression, the nucleus can lose up to 20 % of water. Contrariwise, when the load is reduced, the IVD reabsorbs the fluid in order to reach a new osmotic balance (Johnstone et al., 1992). The viscoelastic behavior of the IVD is thus the result of the interaction between a solid phase (proteoglycans and collagen fibers) and a liquid phase (interstitial fluid composed of water, dissolved gas and small proteins) (Mow et al., 1990). This specific behavior, shared by all biphasic materials, is characterized by a variation of the mechanical response with time during the application of a constant strain or a constant stress: 1) creep is defined by the increase of the strain when a constant stress is applied, 2) stress relaxation by the decrease of the stress when a constant strain is applied.

Modeling of the Viscoelastic Behavior of the IVD

Creep, which is associated by the decrease of the height of the IVD under the application of a constant compressive load, is the most described in the literature. It could be explained by the duality of the IVD composition: a viscous liquid within an elastic material. In rheology, the first one can be associated with a damper mechanism and the second to a spring. The association in series and/or in parallel of two or several of these two elementary units can be used to model the viscoelastic behavior of any living tissue. The Kelvin unit is a rheological model with a spring and a damper in parallel. The three parameters model is defined by a spring (stiffness E_2) in series with a Kelvin unit (Stiffness E_1 and damping η_1). A four parameter model is also proposed with two Kelvin units in series (adding a damping η_2) (see also Figure 10).

Burns et al. (Burns et al., 1984) have shown that the use of a simple Kelvin unit causes prediction errors of 10 to 20 % with respect to the creep test results. Their estimates for the three and four parameters models are relatively equivalent, with lower errors in the first case, but a bigger reliability close to zero in the

second case. Keller et al. (Keller et al., 1987) have made a creep test of 30 minutes under a load of 27 kg, preserving the posterior arches of the vertebrae. They only analyzed the three parameter model, because it can be physically interpreted. Indeed, the first stiffness E_2 is linked with the immediate strain of the IVD under the sudden application of the load; the Kelvin unit then acts to decrease gradually the height of the IVD to a new equilibrium state, but with a decreasing speed (called creep rate). They also noticed, as did Kazarian (Kazarian, 1975), that the rate of creep increases in a very important way (factor two) in the case of the degenerate IVD: this becomes less viscoelastic. In a more recent study, Campana et al (Campana et al., 2011) have performed creep tests of 10 minutes under a load of 400 N, with a posterior arch resection (spinous process, yellow ligament, articular facets). The use of the three parameters model provided an reproduction of the experimental creep with an error of less than 1%. Mean values of creep parameters are reported: 10.2 MPa (min 3.2, max 19.7) for E_1 ; 1.7 MPa (min 0.9, max 3.8) for E_2 ; 4.4 GPa.s (min 1.0, max 9.7) for η_1 . They also underlined the decrease of the viscoelastic properties of the IVD with its level of degeneration. It should be noticed that the creep is responsible for a loss of global height of the IVD between morning and in the evening, with a 18 mm decrease on average for a young person, and of 13 mm for an older person (Natarajan and Andersson, 1999).

Generally speaking the stress relaxation of the IVD was little treated in the scientific literature. Only one study using a rheological model could be found for the relaxation (Holmes and Hukins, 1996). They demonstrated that the four parameter model could describe the viscoelastic behavior of the IVD in relaxation.

Vibration Analysis for the IVD

More recently, experimental protocols were developed to study the damping capacities of the IVD for vibratory conditions (low frequencies) (Asano et al., 1992; Ekström et al., 1996; Izambert et al., 2003; Kasra et al., 1992; Smeathers, 1984). The work of Izambert et al. (Izambert et al., 2003) based on the use of a free mass applied to the superior face of the IVD, has the advantage to reproduce the physiological *in-vivo* conditions. They have shown that the apparent stiffness varies, from 5 Hz to 30 Hz, between 0.19 and 3.66 MN/m and the apparent damping between 32 and 2094 Ns/m. They also found that the average resonant frequency was about 8.5 Hz.

4. Ligaments

Spinal ligaments are non-homogeneous structures with short and long fibers that carry tensile forces along their long axis. They have many different functions in the vertebral column: (i) they allow adequate physiological motion by restricting displacement within safe limits (Zander et al., 2004) (ii) they help the muscles providing stability to the spine within its physiologic ranges of motion thus protecting the spinal cord and (iii) they absorb large amounts of energy in highly dynamic situations.

Experimental data

Data has been published quantifying the nonlinear and anisotropic behaviour of the main human lumbar spine ligaments (anterior and posterior longitudinal ligaments, joint capsules, ligamentum flavum, interspinous, and supraspinous ligaments) in cadaveric specimens (Chazal et al., 1985; Neumann et al., 1992; Panjabi, 1992; Pintar et al., 1992; Shirazi-Adl et al., 1986). These are paramount to properly understand the bone-ligament structural function. Performing biomechanical tests and analysis of the biomechanical properties (stress-strain curve), however, are complicated due to technical challenges in obtaining proper clamping of the samples and the precise determination of strains in the ligaments. The data reported in the literature varies strongly from specimen to specimen, as summarized by (Zander et al., 2004).

Experimental data has also been published on the viscoelastic properties of human lumbar spine ligaments. Yahia et al. (Yahia et al., 1991) for example, performed hysteresis experiments, stress-relaxation and stepwise load-relaxation tests to investigate the time-dependent properties of the interspinous-supraspinous ligament complex, highlighting the necessity to test spinal ligaments in a dynamic way to account for relaxation phenomena. Similarly, Lucas et al. (Lucas et al., 2008) have documented the effect of loading rate on ligament behavior with higher rates leading to stiffer load–displacement behavior and observed that the amount of relaxation is dependent upon the amount of initial stretch (Lucas et al., 2008; Troyer and Puttlitz, 2012; Yahia et al., 1991).

Spinal modeling

These results have been incrementally incorporated into FE models of both the human cervical and lumbar spine with two main applications: (i) impact biomechanics (Du et al., 2014; Laville et al., 2009; Lee and Teo, 2005) and (ii) spinal instrumentation (Little et al., 2007; Park et al., 2013; Pitzen et al., 2001; Schmidt et al., 2012, 2013, Zander et al., 2004, 2009).

These studies show that the intersegmental rotation, and more generally, the ROM of a lumbar motion segment are influenced by the stiffness of the ligaments (Zander et al., 2004). More recently, Ellingson et al. (Ellingson et al., 2016) showed that incremental ligament failure produced increased ROM and decreased stiffness. This increase in mobility was much more pronounced for all directions except lateral bending, which is minimally impacted by ligaments. Overall, computational studies suggest that, if spinal ligaments do not have a dominant mechanical action when studying mobility, they are very important for preventing injury.

Oxland (Oxland, 2016) also highlighted that spinal ligaments are more complex structures than elastic bands, as they are sometimes described. Several studies have described the presence of mechanoreceptors in spinal ligaments (Yahia and Newman, 1993) thereby suggesting an active role beyond simple elastic stabilization of the spinal column. Further, more detailed quantitative anatomy of

spinal ligaments would be a positive contribution to the literature, given the future importance of computational models of the spine.

5. Strain Energy Density Functions used in the literature

The complex behaviour of the Spinal Functional Unit (SFU) can be explained, on one hand, by the geometrical non-linearities and, on the other hand, by the material non-linearities. For the latter, different material models have been proposed and employed in Finite Element Analysis of the spine. The most relevant ones for the Intervertebral disc (ground substance of annulus bulk, nucleus pulposus and fibers of annulus) and spinal ligaments are summarized in table 4 below.

Component	Ground substance of annulus bulk		Nucleus pulposus		Fibers of annulus		Ligaments		
Kim and Park*	Mooney-Rivlin	C10=0.18 C01=0.045	Incompressible fluid-filled cavity		Non-linear dependant on distance from disc center 6 layers - criss-cross pattern		Non-linear stress-strain Strain rate dependent curve		
Puttlitz and Labus*	Yeoh	C10=0.0146 C20=-0.0189 C30=0.041	Linear elastic	E=1.0 v=0.49	Non-linear, two families of fibers	A3=0.03 b3=120.0	Exponential force-displacement curves		
Chen and Wang*	Mooney-Rivlin	C10=0.42 C01=0.105	Incompressible fluid		Non-linear, 12 layers -criss-cross pattern,		Linear stress-strain curve		
Little and Adam*	Mooney-Rivlin	C10=0.7 C01=0.2	Incompressible fluid		Tension-only, embedded linear elastic elements, 8 layers with alternating orientation		Piecewise nonlinear elastic with individual ligament lengths at each spinal level		
Schmidt and Wilke*	Mooney-Rivlin	C10=0.56 C01=0.14	Incompressible fluid-filled cavity		Non-linear stress-strain curve		Non-linear stress-strain curve		
Shirazi-Adl*	Linear elastic	E=4.2 v=0.45	Incompressible fluid		8 layers of fiber-reinforced membranes with through annulus		Collection of uniaxial elements with nonlinear properties		
Rohlmann and Zander*	Neo-Hookean	C10=0.3448 D1=0.3	Incompressible fluid-filled cavity		Non-linear, dependant on distance from disc center, 14 layers - criss-cross pattern		Non-linear stress-strain curve		
Goel and Kiapour*	Neo-Hookean	C10=0.3448 D1=0.3	Incompressible fluid		8 layers of fiber-reinforced continuum elements with criss-cross pattern		Uniaxial 2D elements with nonlinear hypoelastic properties		
Xao	n/a		Mooney-Rivlin	C10=0.12 C01=0.12 D1=1	Mooney Rivlin	C10=0.56 C01=0.14 D1=1	Ogden	ALL, SSL, ISL	$\mu_1=0.177, \alpha_1=3.080,$ $\mu_2=0.627, \alpha_2=13.860, \mu_3=0.357, \alpha_3=-6.800, D_1=1, D_2=1, D_3=1$
								PLL, LF	$\mu_1=0.177, \alpha_1=3.080,$ $\mu_2=0.627, \alpha_2=13.860, \mu_3=0.357, \alpha_3=-6.800, D_1=1, D_2=1, D_3=1$
								ITL	$\mu_1=0.177, \alpha_1=3.080,$ $\mu_2=0.627, \alpha_2=13.860, \mu_3=0.357, \alpha_3=-6.800, D_1=1, D_2=1, D_3=1$
Vacas	Reduced polynomial	C10=0.0054 C01=0.98 D1=5.60 D2=0	Mooney-Rivlin	C10=0.12 C01=0.09	Tension only nonlinear elastic (Ezquerro et al. 2007)		tension-only non-linear elastic with an exponential toe-in followed by a linear region		
Mustafy	Mooney Rivlin	C10=0.18 C01=0.045	Linear elastic	n/a	Non-linear elastic curve		ViscoElastic properties (Time dependent Prony series parameters extracted from Sadeh et al. 2000)	ALL	E=11.4
							PLL	E=20.4	
							ISL	E=25.3	
							IL	E=17.1	
							CL	E=7.7	
							LF	E=27.2	
Clouthier	Reduced Polynomial	C10=0.025 C20=0.625 D1=1.224	Neo-Hookean	C10=0.04 D1=0.096	n/a		n/a		
Zhu	Neo-Hookean	C10=0.3448 D1=0.3	Incompressible fluid		(Shirazi-Adl et al., 1986)		Non linear (Rohlmann et al. 2006)		
Laville	Linear elastic	E=2.5 v=0.4	n/a		Ant-post Linear elastic tension only	E=110	Linear elastic	ALL	E=10 s=1
								PLL	E=20; s=1
								LF	E=25 s=0.4
								ISL	E=3 s=1.2
								PC	E=60 s=1.2
								AC	E=60 s=1.2
Prudhomme	Multilinear	v=0.45	Linear elastic	E=1 v=0.499	Linear elastic	E=2000 s=1	Linear elastic	ALL	E=162 s=74
								PLL	E=20; s=20
								LF	E=26 s=84
								ISL	E=50 s=20
								PC	E=1 s=40
								AC	E=1 s=20

Table 4: Summary of the main material models of soft tissues used in the Finite Element Analysis of the spine. HyperElastic material models have been highlighted in grey. The following SI units have been used: MPa, mm², MPa⁻¹. The following acronyms have been used for the ligaments: Anterior Longitudinal Ligament (ALL), Posterior Longitudinal Ligament (PLL), Intertransverse Ligament (ITL), Ligamenta Flava (LF), Interspinous Ligament (ISL), Supraspinal Ligament (SSL), Posterior Capsule (PC), Anterior Capsule (AC). *: adapted from (Dreischarf et al., 2014).

For convenience, we remind the reader the general forms of the hyper-Elastic Strain Energy Density functions W employed in the table above:

Neo Hookean

$$W = C_{10}(\bar{I}_1 - 3) + \frac{1}{D_1}(J - 1)^2$$

Mooney-Rivlin

$$W = C_{10}(\bar{I}_1 - 3) + C_{01}(\bar{I}_2 - 3) + \frac{1}{D_1}(J - 1)^2$$

Reduced Polynomial

$$W = C_{10}(\bar{I}_1 - 3) + C_{20}(\bar{I}_2 - 3) + \frac{1}{D_1}(J - 1)^2 + \frac{1}{D_2}(J - 1)^4$$

Yeoh (incompressible)

$$W = C_{10}(I_1 - 3) + C_{20}(I_1 - 3)^2 + C_{30}(I_1 - 3)^3$$

Ogden

$$W = \sum_{i=1}^n \frac{\mu}{\alpha_i} (\bar{\lambda}_1^{\alpha_i} + \bar{\lambda}_2^{\alpha_i} + \bar{\lambda}_3^{\alpha_i} - 3) + \frac{\kappa}{2}(J - 1)^{2i}$$

Where:

- I_1, I_2 and J are principal invariants of the right Cauchy-Green tensor $C = F^T \cdot F$; we recall that $I_1 = \text{tr}(C)$, $I_2 = \frac{1}{2}[(\text{tr}(C))^2 - \text{tr}(C^2)]$ and $J = \det(C)$ and F is the deformation gradient.
- λ_1, λ_2 and λ_3 are the principal stretches.
- $\bar{\cdot}$ is associated with the deviatoric part of C ; $C_{dev} = J^{-\frac{2}{3}}C$.
- C_{ij}, α_i, μ (ground shear modulus) and κ (bulk modulus) are the material parameters.

6. Discussion

A detailed knowledge of the fundamental biomechanics of the spine is a basic requirement for proper management of various spinal disorders, effective injury prevention and rehabilitation as well as for realistic testing of spinal implants and adequate loading of *in-vitro* studies (Dreischarf et al., 2016). Under the impulse of the prevalence of clinical problems of the human spine (low-back pain, sciatica, spinal deformity, spinal tumors, and spinal injury), biomechanical research on the spine has expanded at rapid pace during the last decades, as summarized in the publication of the 2nd edition of White and Panjabi's textbook, *Clinical Biomechanics of the Spine* in 1990 and, more recently, in the review paper by (Oxland, 2016).

Driven by the ever-growing computer power and imaging devices, the development of FE models has become widespread and have allowed to overcome some of the existing shortcomings (invasiveness, complexity of the organization of the biological tissues in the spine and complexity of establishing the loads present in the human spine), and limited numbers of available subjects. Computational models have thus emerged as powerful and reliable tools with considerable applications in surgery planning, in studying the etiology, progression and effects of spinal deformities, intervertebral disc (IVD) degeneration or studying crash injuries, just to name a few. These models have enhanced our understanding of the spine and will continue to do so in the future, especially with the increasing computation power.

In our group, numerical work performed using FE modeling has highlighted the paramount influence of both geometric patient-specific modeling and *in-vivo* personalization of tissue mechanical properties. More specifically, (Laville et al., 2009) showed, with 16 subject specific FE models, that geometric inter-subject variability explains a major part of the motion variability at least in lateral bending and axial rotation. Ultrasound elastography has also successfully been used in our group to assess the mechanical properties of intervertebral disc both *in-vitro* and *in-vivo*. This represents a novel biomarker for spine pathologies and a key tool for *in-vivo* personalization of tissue mechanical properties.

There are many exciting avenues for future research. Amongst these, the question of the validation of computational modeling and simulation with the perspective of supporting the development of medical devices is central. As highlighted by the US Food and Drug Administration (FDA), there is currently a lack of consistency and predictability of the review of computational models that hinders their use for the evaluation of the safety and effectiveness of medical devices.

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References

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