Epilogue

Low-back pain poses a huge burden on society and on the individual patient, and extensive research has been and is currently conducted into the pathophysiology, aetiology, epidemiology and biomechanics of spinal disorders. In addition, clinical practice advances with new (minimally invasive) surgical techniques, instruments, implants and tissue engineering strategies. Although not all new therapies are equally successful, advancements are good news for the patient. On the other hand, they also shed light on a fundamental problem that needs to be solved; a dearth of valid diagnostic tools to determine the underlying cause of low-back pain in the individual patient.

The aim of this thesis is to study structural vibration testing of the lumbar spine for the assessment of segmental stiffness and to examine whether this methodology may be developed into a clinical tool for the diagnosis and evaluation of treatment of low back pain and degenerative spinal deformations. Structural vibration testing is considered a promising technique to study spinal mechanics since it is non-destructive and safe given the small loads and deflections needed for the investigations.

Clearly, progress is made in small steps; this thesis describes the first steps towards the development of a novel diagnostic method. All the experiments in this thesis were performed in a controlled in vitro condition using human and goat mono- and poly segmental spinal sections, with no complicating contributions of the surrounding tissue. In this final chapter the preceding chapters will be revisited shortly and recommendations for future efforts are given.

PROBLEMS IN DIAGNOSING CAUSES OF LOW-BACK PAIN

It’s an obvious fact that in order for a therapy to be effective, it must target the underlying problem. However, indications for treatment of spinal disorders are difficult to obtain. As described in Chapter 1, typical diagnostics rely on physical examination, occasionally extended with imaging. With these techniques, a specific
diagnosis is made in only 10% of the cases [120]. Moreover, while many interventions address the mechanical properties of the joint, these are not measured or are not measured accurately. Chapter 2 examines the measurement error that might result from using current per-operative measurement devices that take only the loading and deflection of a single segment into account. A stochastic mechanical model was constructed to investigate the effect of measuring an isolated single segment compared to measuring a single motion segment in an intact spine. The study showed that stiffness estimates obtained by loading a single segment in an intact spine are highly correlated with actual stiffness, but overestimate stiffness by a median of 18%. Moreover, the stiffness within degenerated spines was shown to vary largely, which can cause errors up to 400%, and might lead to erroneous surgical decisions. Clearly, better methods have to be developed for diagnostics. In addition, these diagnostics need to be applicable non-invasively, being able to judge beforehand whether the patient might benefit from surgical intervention, i.e. decide if the symptomatic segment shows mechanical dysfunctioning that can be targeted by restoration of stiffness, or that other interventions or conservative treatment have to be considered.

In line with this reasoning, it was previously attempted to design a tool to assist surgical decision-making in a group of patients with incapacitating low-back pain that were considered for spinal fusion. Patients had undergone diagnostic tests, such as radiographs, magnetic resonance imaging and provocative discography; however, it remained unclear whether patients would benefit from spinal fusion. Therefore, additional tests were performed such as the pantaloon plaster cast test and/or temporary external transpedicular fixation (TETF) of the lumbar spine. Pantaloon plaster casting implies that a cast is applied to patients from the nipples down to the waist and extending over one leg to the knee. After 6 weeks in this corset, patients are asked whether they had experienced less pain, and thus might benefit from fusion surgery. In TETF, screws are inserted through the skin in the vertebrae under and above the painful disc under general anaesthesia, and joined by a bar to provide temporary fusion. After 10 days, the TETF is removed and patients should report adequate pain relieve during fixation and definitely less pain relieve during non-fixation (placebo trial) to be eligible for spinal fusion. However, both the pantaloon test and TETF were found to have limited or no value in predicting a favourable outcome of lumbar fusion [121-123].
STRUCTURAL VIBRATION TESTING OF THE LUMBAR SPINE

In Chapter 3 the feasibility of structural vibration testing for the assessment of intervertebral stiffness was examined. Previous studies were able to measure the presence of structural damage in the spine, but could not relate specific changes in the vibration data to a specific type of damage [60]. This information is likely present in the vibration data but requires analysis of the modal parameters. To study the modal characteristics of the spine, goat single motion segments without muscle tissue were tested in vitro. Large structural disruptions were created consecutively by removing the ligaments and creating a hole in the annulus fibrosus. The results showed that removal of the ligaments caused no significant difference in the mode shapes and eigenfrequencies, but the hole in the annulus decreased the eigenfrequency of the torsion mode, thus torsion stiffness. This study also showed that a motion segment, which is not a linear structure, behaves linear if only small forces and deformations are applied. This implies that structural vibration tests and modal analysis techniques can in principle be applied in the spine.

Although the type of structural damage was identified successfully in Chapter 3, this does not mean that vibration analysis can also be applied to human motion segments with structural alterations that occurred naturally. Firstly, degenerative changes might make the behaviour of the motion segment nonlinear, even for small deformations. For example chondrosis intervertebralis, which manifests itself as a decrease in water content of the nucleus pulposus and the appearance of a dry crumbling mass, reduction of elasticity of the disc, development of tears in the annulus fibrosus and calcification and ossification in the area of the nucleus pulposus [8], might result in “stick-and-slip” behaviour and friction during vibration testing. Osteochondrosis intervertebralis, in which also disc height is lost, might cause nonlinearities by impacting of the facet joints during vibration. Secondly, damping might be larger in human segments than in goat segments, making it difficult to obtain the eigenfrequencies and corresponding mode shapes from the frequency response function (FRF).

In Chapter 4, structural vibration tests were performed on human motion segments. The specimens were tested under similar conditions as in Chapter 3, but the segments were also tested quasi-statically to obtain ‘gold standard’ static stiffness values. The results showed clear frequency response peaks indicating that vibration testing is also
feasible in human motion segments. In addition, an increase in the force amplitude by a factor two resulted in an equally large increase in the response amplitude, indicating that the system behaved linearly. Moreover, the eigenfrequencies were significantly correlated to the static stiffness values, which is an important finding since it suggests that eigenfrequencies provide a valid measure of segmental stiffness. A second important implication of the correlation between static stiffness values and eigenfrequencies is that it shows that eigenfrequencies have the potential to discriminate between different levels of degeneration just as static stiffness values can. The advantage of eigenfrequencies over static stiffness values is that eigenfrequencies can be obtained with small forces and deformations and might therefore offer a safe approach for assessment in patients.

Since Chapter 3 and Chapter 4 showed that the presence of specific structural damage can be assessed with vibration testing and modal analysis, the next step was locating the damage. Eigenfrequencies can only reveal the presence of damage; localizing damage requires modal analysis and parameter estimation techniques, especially when baseline stiffness information is not available. Different parameter estimation techniques exist, some of these techniques directly fit the experimental and the analytical data using a random polynomial, others use an indirect approach assuming an underlying relation between parameters. The optimal fit is achieved iteratively by minimizing the difference between the two sets of data. A commonly used parameter estimation technique is an indirect approach in which the experimental FRF is fitted to the numerical FRF by adjusting the parameters in the equations of motion. An alternative is the model-updating approach that was used in this thesis, in which the FRF is used to derive eigenfrequencies and mode shapes, which are then fitted to the analytical modes shapes and eigenfrequencies. Model updating allows the use of a reduced analytical model that does not contain more points and degrees of freedom than can be measured experimentally; in this thesis we aimed at using the simplest possible model to describe the modal characteristic of the spine with sufficient precision, to be able to identify damaged motion segments from outliers in the stiffness matrix (see Appendix 1). Although it is possible to build a more complex model, an increase in the amount of model parameters will also result in an increase in model outcomes, while not all outcomes will be physically meaningful.

An analytical model is constructed based on material properties and geometrical
information. Chapter 5 describes how model parameters of the lumbar spine can be obtained from quantitative computed tomography. A sensitivity analysis was performed to establish the necessary accuracy of the model parameters to ensure successful estimation of the values for bending stiffness. The sensitivity analysis revealed that the modal parameters for bending of the model were most sensitive to changes in vertebral height and mass and joint stiffness. This implies that the presented model can be used for model updating of the stiffness matrix, provided that the parameter values for vertebral height and vertebral mass are sufficiently accurate.

Chapter 6 describes the actual model updating procedure. The lumbar spines of six Dutch milk goats were injected with chondroitinase-ABC to create mild degeneration at random levels, their lumbar spines were harvested and the spinal mechanics were tested statically and dynamically. Vertebral height could be measured on magnetic resonance images; vertebral mass was calculated from vertebral height, based on the relation between mass and height that was found in the previous chapter. These subject specific values were used to parameterize the model, as well as average values over six goats from the previous chapter for inertia and location of the vertebral centre of mass. Unfortunately, model updating resulted in a suboptimal fit between experimental vibration data and numerical vibration data as was assessed with the Modal Assurance Criterion (MAC) and the residual of analytical and experimental eigenfrequencies. Most likely this was due to inaccuracies in the estimated vertebral mass. The segmental levels with the lowest estimated stiffness values corresponded in 50% of the cases to the levels with the lowest static stiffness, which means that it is not possible to identify the degenerated levels with sufficient certainty. Although these results were disappointing, they also indicate that the proposed methodology can work, provided that better estimates of vertebral mass are obtained.

**FUTURE EFFORTS**

Future efforts should first be directed towards the improvement of the fit between experimental and numerical data, second, towards a measurement set-up that resembles in vivo conditions and third towards measurement methods that can be applied non-invasively. Considering the improvement of the fit, basically, three topics can be identified: (i) improvement of experimental data, (ii) improvement of the penalty function, (iii) reduction of model parameter error and model structure error.
**Improvement of experimental data**

Improvement of the experimental data can be achieved by reduction of the measurement error during experimental vibration tests. This is not trivial; performing vibration tests requires careful preparation of the tests, skilful use of the measurement equipment and well thought-out expectations of the measurement outcome to be able to reflect on the measurement quality. Moreover, there are no confidence intervals that can be assigned to test data uncertainties. As was summarised by Mottershead and Friswell [124], measurement error can originate from the dynamic characteristics of the equipment that is used to perform the vibration tests, such as the mass of the shaker and the stiffness of the stinger. Piezoelectric transducers such as force transducers tend to lack linearity at low frequencies and may be sensitive to temperature, and magnetic and acoustic fields. Electronic systems generally introduce low levels of instrument noise. Roving accelerometers commonly cause errors in the eigenfrequencies, and transverse and base bending of accelerometers and accelerometer cable noise are also known error sources. During data processing, especially with multi-frequency excitation and fast Fourier transformation techniques, errors can arise from aliasing, spectral leakage and linearization of non-linear effects. Finally, modal analysis, especially curve-fitting methods, require user intervention which might introduce additional imprecision during derivation of the modal characteristics from the experimental data.

During the experiments in this thesis, possible measurement errors as mentioned by Mottershead and Friswell were prevented as much as possible. For example, experience with accelerometers in Chapter 3 learned that goat vertebral mass is relatively low (30-83 grams) compared to the weight of the accelerometers (1 gram). In multisegmental specimens, the length of the specimen in combination with the weight of the accelerometers could have caused errors in the eigenfrequencies; therefore, in Chapter 6, laser-Doppler vibrometry was used. Further reduction of measurement error might result from a more dedicated suspension of the shaker and the attachment of the shaker to the specimen. However, typical free-free measurement conditions in which the structure is suspended from rubber bands seem unsuit for the assessment of the spine, since the eigenfrequencies of the suspension lie in the same frequency band as the resonances of the spine. On the other hand, boundary conditions in which the specimen is clamped at one or two sides and attached to a shaker might produce the effect of a ‘follower force’; a displacement dependent change of loading. Base-excitation in which the excitation is provided by the table the specimen is mounted
to was not tested here, but might provide an interesting alternative measurement set-up for in vitro measurements since it makes shaker attachment to the specimen superfluous. A drawback from base-excitation might be that not all modes can be excited as easily.

The experimental data might further improve from on line assessment of measurement outcome. During the experiments described in this thesis, on line feedback was available on the FRF and coherence, but also information on the eigenfrequencies and mode shapes and how these relate to the analytical modal characteristics that were previously obtained from finite element modelling might help to improve data acquisition. Especially the occurrence of complex mode shapes in the experimental data requires attention. In complex modes, the relative phasing of the modes is not either exactly in-phase or out-of-phase. This typically occurs when damping is not related to the mass and the stiffness of the system. In the spine, non-proportional damping might originate from degeneration as discussed previously, but complex modes might also be caused by an improper measurement set-up.

Finally, improvement of the experimental data might also be achieved by increasing the amount of data. For example, by testing the same structure using multiple boundary conditions or repeating tests with different amounts of known mass added to the structure [124].

**Improvement of the penalty function**

The penalty function aims to minimize the difference between the experimental and numerical data, and usually includes mode shapes and eigenfrequencies. In Chapter 6 the penalty function contained a mix of the methods described by Nash who minimized a weighted sum of eigenvalues and eigenvectors [125], and Grossman who maximized a correlation coefficient based on a weighted average of the ratio of measured and analytical eigenfrequencies and the $MAC$ between the measured and analytical mode shapes [126]. In model updating, a sensitivity matrix is frequently included in the penalty function. The sensitivity matrix contains the first derivatives of the eigenvalues and the mode shapes with respect to the parameters [124]. Fox and Kapoor formulated a much used sensitivity-based model updating method [127] from which also model updating in the spine might benefit.
Reduction of model parameter error and model structure error

As mentioned previously in Chapter 6, reduction of model parameter errors, such as vertebral mass, improves the correlation between experimental and numerical data, but also the model structure might be improved. Errors in model structure occur e.g. by (over)simplifying the structure, neglecting particular properties, assumptions concerning boundary conditions and assumptions about joints. Two properties that were examined only briefly and need further investigations to definitely omit them from, or add them to, the model are transverse shear deformation and damping.

The transverse stiffness of one goat segment (T13-L1) was measured in a pilot study by exerting a shear force on the bottom vertebra and restraining the top vertebra. Each measurement was performed three times, and the stiffness was calculated roughly from the linear part of the load-deformation curves (anteroposterior stiffness, 378, 399 and 413 N·mm⁻¹; posteroanterior stiffness, 329, 327 and 333 N·mm⁻¹; mediolateral stiffness, 261, 301 and 310 N·mm⁻¹). Although these measurements provide only a crude estimate of translational stiffness, they indicate that the eigenfrequencies corresponding with shear modes are probably higher than for bending modes, since the angular stiffness is on average 11 N·m·rad⁻¹ for flexion-extension and 7 N·m·rad⁻¹ for lateroflexion. NB in torsion, shear plays an important role. Although it is not probable that shear modes were mistaken for bending modes in this thesis, in future measurements this can be assured by measuring the deflections of points on the vertebra that are aligned along the longitudinal axis of the vertebra. With these data, rotational and translational motions can be distinguished. When eigenfrequencies for transverse motion appear within the frequency band of rotation, transverse stiffness can easily be incorporated in the model.

Damping is present in the spine, but was assumed to be proportional and small, and therefore not to interfere with the fitting procedure in Chapter 6. However, high values of viscous damping might influence the location of the eigenfrequencies and the extraction of the modes from the test data. Note that for a one degree-of-freedom system, in case of proportional viscous damping, the damped frequency \( \omega_d \) is related to the undamped eigenfrequency \( \omega_0 \) and the damping ratio \( \zeta \) according to:

\[
\omega_d = \omega_0 \sqrt{1 - \zeta^2}
\]  \hspace{1cm} (7.1)
High values for damping would therefore result in an overestimation of the analytical eigenfrequencies when damping is not correctly incorporated in the model. During the fitting procedure, this would result in an overestimation of mass or in an underestimation of stiffness. Damping can be derived from the measurements in several ways. For example, the damping ratio can be obtained from the FRF according to Equation 7.2, where \( \omega_0 \) is the eigenfrequency and \( \omega_1 \) and \( \omega_2 \) represent the frequencies on either side of \( \omega_0 \) at \( 1/\sqrt{2} \) times the peak height:

\[
\zeta \approx \frac{\omega_1 - \omega_2}{2\omega_0}
\] (7.2)

In an unpublished pilot study, we measured damping ratios and attempted to correlate these to degeneration scores. 14 naturally degenerated L5-L6 and L6-S1 Beagle motion segments and six L2-L3 and L4-L5 human motion segments were impacted with a hammer to excite forward bending and the logarithmic decrement was calculated from the motion response, assuming a one degree-of-freedom system. For the Beagle segments, the degeneration scores from macroscopic observations were all 2 (mild degeneration) except two segments that scored 3 (advanced degeneration). For the human segments, the Pfirrmann scores from magnetic resonance imaging were 4 (advanced degeneration), one segment scored 3 (mild degeneration) and one segment scored 5 (severe degeneration). The damping ratios for the human segments were 0.48 for degeneration score 3, 0.16-0.27 for score 4 and 0.13 for score 5. For the Beagle segments the damping ratios were 0.10-0.23 for score 2 and 0.15-0.22 for score 3. The damping ratios were higher than previously reported values between 0.05 and 0.15 for human motion segments [50, 110, 128], although comparison between different studies has to be done with care due to differences in measurement methodology. Based on Equation 7.1, the damping ratios from the pilot suggest that damping might have a substantial effect on the modes and should be included in the analytical model. Of course, these results are preliminary, and in contrast with previous reported results. However, assessment of damping can easily be incorporated in vibration experiments, and if needed, the analytical model might be extended with parameters for damping. The results do not point toward cut-off values that discriminate between different phases of degeneration. As with stiffness, the relation between degeneration and damping is probably subject-specific.
In vivo measurements conditions

In the more distant future, efforts should be directed towards a measurement set-up that resembles in vivo conditions in which the lumbar spine is attached to the thoracic region and the sacrum and pelvis. Whether this attachment has to be fixed-fixed, or that the thoracolumbar and the lumbosacral junction are better represented by springs and the upper and lower body by large masses as was done by Keller et al. [110] should be part of the investigations. Also the presence of surrounding (inactive) spinal muscles and ligaments and the presence of visceral organs has to be examined. Takashima et al. proposed to incorporate anthropometric data on muscles and viscera into the spine model by adding masses to the vertebrae at a distance anterior to the vertebrae [116]. Kitazaki and Griffin proposed a method based on their earlier work and the work of Belytschko and Privitzer, in which the viscera below T10 were not rigidly attached to the spine but with spring elements, to model to local motion of the viscera that might affect the dynamic response of the whole body [113, 129]. Also Valentini used this method to add the viscera to the spine model [114]. These studies aimed to investigate the effect of whole body vibrations on spinal damage, and further research is needed to decide on the best approach for the purpose of developing a diagnostic tool.

Furthermore, the use of non-invasive measurement methods should be explored. Non-invasive manual and instrumented excitation of the spine is used by chiropractors and manual therapists and the methodology can likely be adjusted for the purpose of diagnosis. The vibration response of the vertebrae can likely be measured with ultrasonography and Doppler imaging, based on the results of a previous study that examined the laxity of the sacroiliac joint [130, 131]. Although the methodology should be adjusted for the measurement of the frequency response of spinal motion segments, these studies show that it is possible to obtain a velocity signal of the moving bone.

CLOSING REMARKS

Both experiments and models address only a part of the ‘real’ world. They are both a tool to gain knowledge about this world by simplifying its characteristics and reducing its number of parameters. In that sense, both experimental outcome and modelling outcome are influenced by the assumptions that are made by the investigator. In this thesis, the complexity of the spine was reduced to a system containing just springs and
masses. Using this simplification, this thesis was able to show that structural vibration testing and modal analysis is feasible in the lumbar spine and that it is a reliable and valid method to obtain damage-specific information on segmental stiffness, also in naturally degenerated segments. Although it was not possible to localize degenerated segments within the spine, this thesis does show a feasible approach for such a measurement method and it shows plausible directions for further improvement of the methodology. In conclusion, this thesis shows that structural vibration testing of the lumbar spine can be used for the assessment of segmental stiffness and this methodology may be developed into a clinical tool for the diagnosis and evaluation of treatment of spinal deformities, degenerative disc disease and low-back pain.
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