

Exploring Growth Plate Morphological Evolution : A Computational Mechanobiological Perspective

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Résumé — This research primarily investigates the relationship between trabecular bone patterns within the vicinity of the growth plate and associated morphological changes, specifically regarding the shape modifications and adaptations to mechanical stimuli. To address this, a finite element model was constructed and compared using medical images. The model was tested first with a generic growth model case and subsequently extended to a clinical scenario involving pathologies such as hip dysplasia.

Mots clefs — Growth plate, bone remodeling, bone development, growth pathologies.

1 Introduction

The study of growth plate biomechanics is a developing field dedicated to exploring the processes governing bone growth and maturation. Located at the ends of long bones, the growth plate is responsible for longitudinal growth and is essential for proper musculoskeletal development, depending on both mechanical and biological factors. However, injuries and diseases affecting the growth plate can disrupt normal bone growth, leading to some pathological conditions like slipped capital femoral epiphysis (SCFE), Legg-Calve-Perthes disease (LCPD), or Hip dysplasia (HD) can alter the mechanical conditions around the growth plate, impacting the endochondral growth process. Advanced imaging and computational modeling provide valuable insights into the biomechanical forces and microstructural changes in the growth plate during both typical growth [1] and disease progression [2]. The role of growth plate shape is significant for load-bearing, especially for handling high shear stresses. [3] demonstrated how mammillary processes adapt for biomechanical stability, while [4] explained how changes in growth plate shape can prevent shear stress-induced failure. However, there is currently no model to predict changes in the growth plate's shape. This study presents a new model for endochondral growth, focusing on the role of trabecular patterns in growth plate development. This model aids in understanding growth plate disease mechanisms and developing more effective treatments, particularly addressing the mechanical factors at each developmental stage. This growth plate development model is rooted in a bone remodeling approach using strain energy density as the primary stimulus controlling bone formation and resorption [5], [6]. For the cartilaginous zones, the model relies on the osteogenic index (OI) [7], determining the strain related to proliferation and hypertrophy during endochondral growth in the epiphyseal plate. Notably, this study marks the first application of a bone remodeling scheme to investigate localized load transmission and its effect on the growth plate's shape and subsequent remodeling.

2 Methods

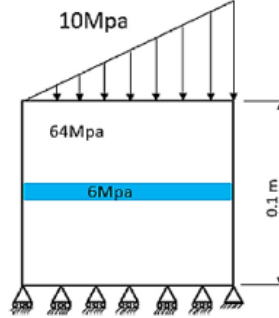


Figure 1– Generic model growth

In the initial phase of our methodology, we propose a new growth model with domain and boundary conditions for bone remodeling and in addition, endochondral growth (figure 1). This work is based in a bone remodeling approach pioneered by [5] and developed later in [8]. This approach hinges upon the utilization of strain energy density as the governing stimulus that orchestrates the intricate processes of bone formation and resorption. To facilitate the practical implementation of this theoretical framework, we used ABAQUS 2017, employing a user element subroutine (UEL). Here, we introduce a modified bone remodeling algorithm that incorporates a strain tensor that depends on the osteogenic index. Notably, the model assumes a linear isotropic behavior for both bone and cartilage materials. Importantly, the strain energy density serves as the primary regulatory stimulus governing the bone remodeling process. The algorithm for the morphological evolution can be seen in figure 2. Firstly, the elastic problem is defined by (1), which establishes the equilibrium between the gradient of the stress field σ and the body forces (b). This equation is coupled with the evolution law presented in (2), where the dimensionless bone density (λ) depends on the strain energy per unit volume (U) at the finite element, along with a reference strain energy (U_{ref}), which serves as the threshold for bone formation or resorption. Additionally, the parameters (k_1) and (n) represent the constant of remodeling speed and an experimental exponent, respectively. This process is iterative, and at each step the elastic modulus (E) is updated following the power law shown in (3) until a convergence criterion is achieved. For the cartilaginous zones, the evolution law is based on the osteogenic Index (OI) [7] which will determine the imposed strain ($\dot{\epsilon}$) due to proliferation ($\dot{\epsilon}^p$) and hypertrophy ($\dot{\epsilon}^h$) due to endochondral growth in the epiphyseal plate that will be imposed in the direction n , perpendicular to the front of ossification, following the evolution law shown in (4), in this equation, the growth constant k_2 is based on the experimental works of [9-11] to achieve same orders of magnitude for the growth long bones in μm per day. It is important to note that the daily elongation may vary for different bones. Finally, the OI depends on the hydrostatic stress (P), the octahedral shear stress (S) and an empiric constant (k_{OI}) as seen in (5).

$$\nabla^T \sigma + b = 0 \quad (1)$$

$$\frac{d\lambda}{dt} = k_1 \left[\lambda^{n-1} \frac{U_{str}}{U_{ref}} - 1 \right] \quad (2)$$

$$E_{t+1} = E_t \lambda^n \quad (3)$$

$$\dot{\epsilon} = (\dot{\epsilon}^h + \dot{\epsilon}^p) n \otimes n = k_2 OI n \otimes n \quad (4)$$

$$OI = S + k_{OI} P \quad (5)$$

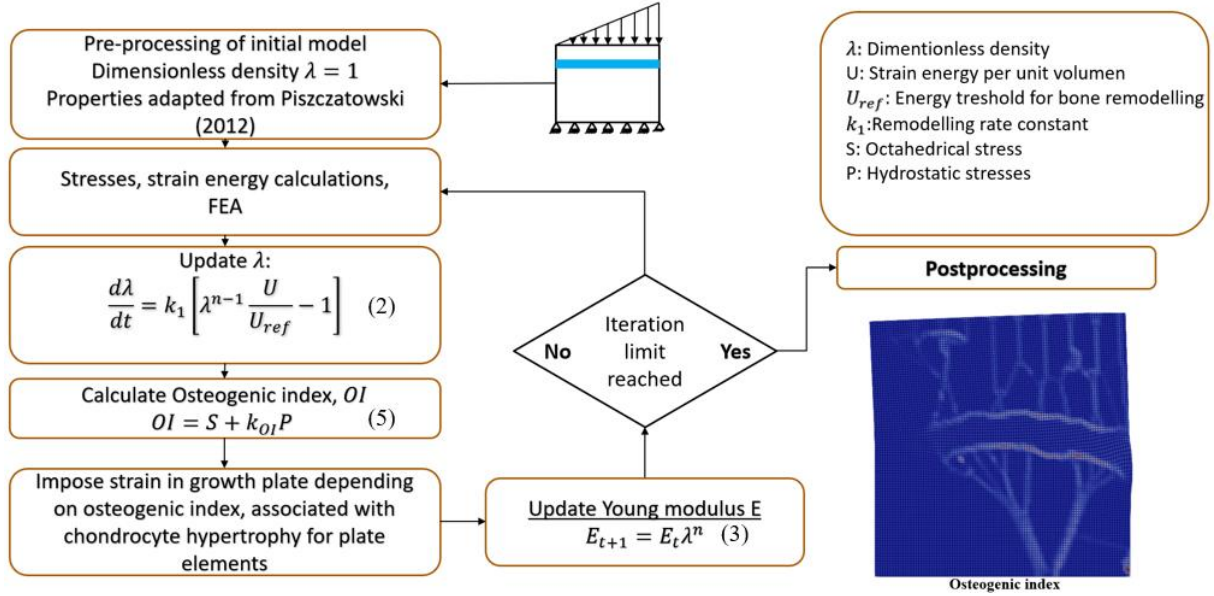


Figure 2 – Modified bone remodelling algorithm, benchmark test, distributed load on a rectangular plate

To calculate the osteogenic index we begin from the principal stresses for the Cauchy stress tensor, as shown in (6):

$$\sigma_{ij} = \begin{bmatrix} \sigma_{11} & 0 & 0 \\ 0 & \sigma_{22} & 0 \\ 0 & 0 & \sigma_{33} \end{bmatrix} \quad (6)$$

$$\sigma_{oct} = \frac{1}{3} (\sigma_{11} + \sigma_{22} + \sigma_{33}) \quad (7)$$

$$\tau = \frac{1}{3} [(\sigma_{11} - \sigma_{22})^2 + (\sigma_{22} - \sigma_{33})^2 + (\sigma_{33} - \sigma_{11})^2]^{\frac{1}{2}} \quad (8)$$

The osteogenic index has been chosen for its capacity to weight both the deviatoric and volumetric components of the Cauchy stress tensor in a single scalar that characterizes each finite element. In this case, the hydrostatic σ_{oct} and octahedral shear stresses τ , as seen in 7 and 8 which depend on the principal stresses σ_{ii} can also be expressed in terms of the invariants of the stress tensor, here we show them in terms of the principal stresses. σ_{oct} is responsible for the volumetric change and it has been seen that this type of stress tends to preserve the cartilage phenotype in the domain whereas τ is responsible for the shape change of the finite element (deviatoric stress) and tends to promote ossification [12].

In the methodology, we employed the generic model for growth depicted in Figure 1. This model, as previously shown, involves an iterative process where bone properties evolve in response to strain energy. Additionally, a strain tensor, influenced by the osteogenic index, is applied. This leads to localized bone formation and alters the shape of the growth plate. To tune parameters such as the osteogenic index constant K_{OI} that determines the growth rate in the growth plate we used the benchmark test shown in figure 3. Once these growth rates were compatible to those found in literature and we had topologies similar to those found in medical images of the growth plates of long

bones, we tested the model in other medical cases shown in figure 5. Here we obtained some features such as the mamillary processes (small bone protrusions found in the interface of the growth plate with trabecular bone) that respond to the localized load transmission of trabecular groups. We took as study cases the development of hip dysplasia and the ossification patterns in the growth plate in mice by examining different μ CT scans to see how ossification bridges coincide with zones of high shear stress, the different images stacks were reconstructed in 3DSLICER, nonetheless a plane stress of the middle section was taken to construct the meshes.

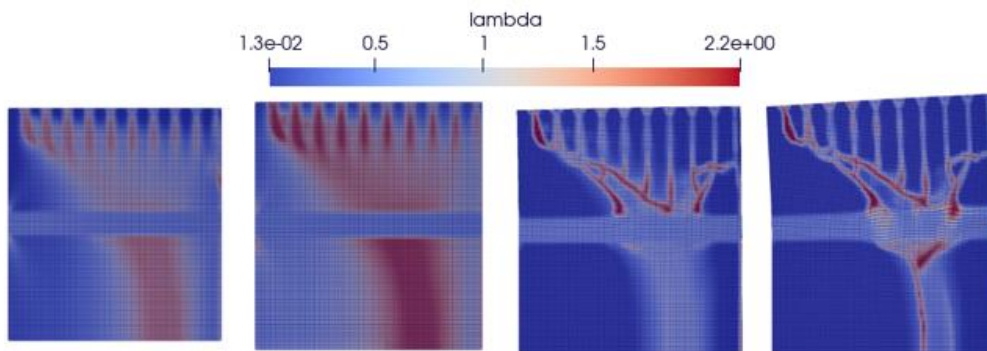


Figure 3 – Generic growth model (Benchmark) test for the evolution of growth plate topology given some trabecular.

Furthermore, for every mesh utilized in the finite element model, we conducted a convergence study, an example is shown in figure 4. This approach allowed us to determine whether the topology results were influenced by the mesh's refinement level. We adopted a convergence criterion with a tolerance of 5% for the normal stresses.

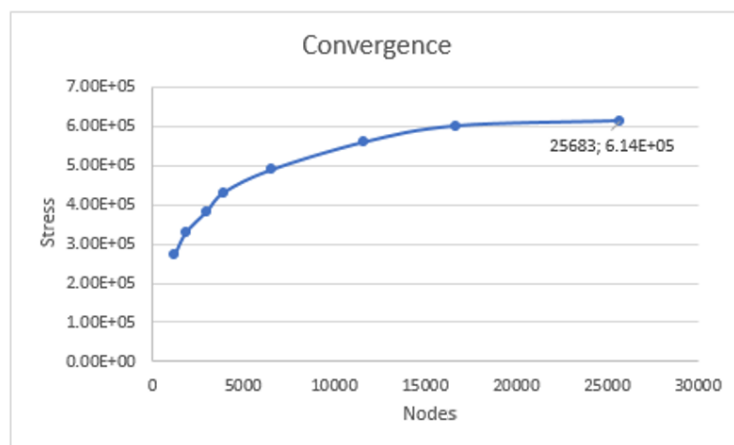


Figure 4 – Convergence analysis for hip dysplasia case.

3 Results

The proposed model shows the evolution of the growth plate according to the mechanical action of the main trabecular groups, seen in figure 5. The evolution of the growth plate for the case of hip dysplasia, and the posterior ossification is seen. Finally, medical images are used to test the proposed method in a patient specific geometry by comparing the final topologies obtained in a qualitative manner, mainly, if ossification bridges correspond to ossifications bridges. In figure 6 a comparison between the trabecular patterns and the maximum shear stress is shown to remark how ossification bridges form, here high-density zones are mainly found in the peripheral part, where ossification

starts to appear in development. This behavior is also shown in the tibial plateau of a 2-month C57BL6 mice, shown in figure 7, where the ossification bridges correlate clearly with high shear zones. In figure 8 the maximum average shear stress along a path on the growth plate shows a clear correlation between high shear stresses and ossification bridges.

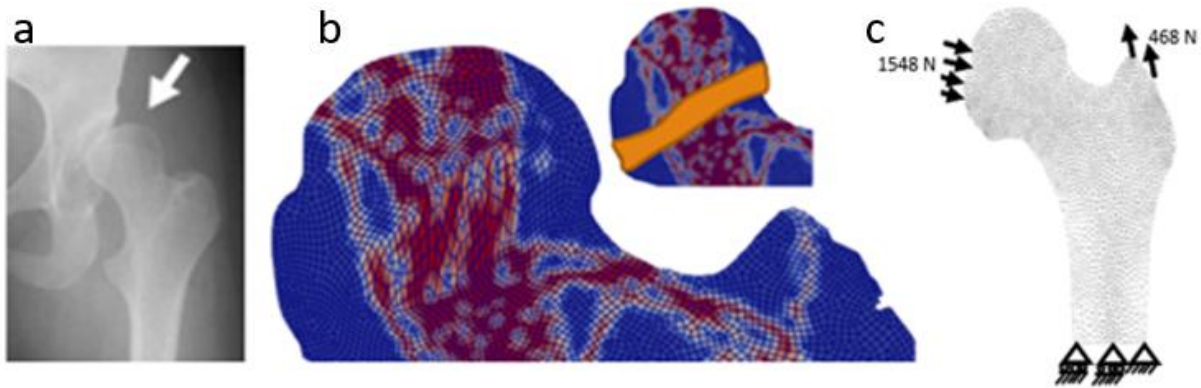


Figure 5 – a) Hip dysplasia in a skeletally mature individual [2] b) Evolution of a femur in hip dysplasia (ABAQUS 2017) c) Boundary conditions according to [13], femoral load is modified to be horizontal

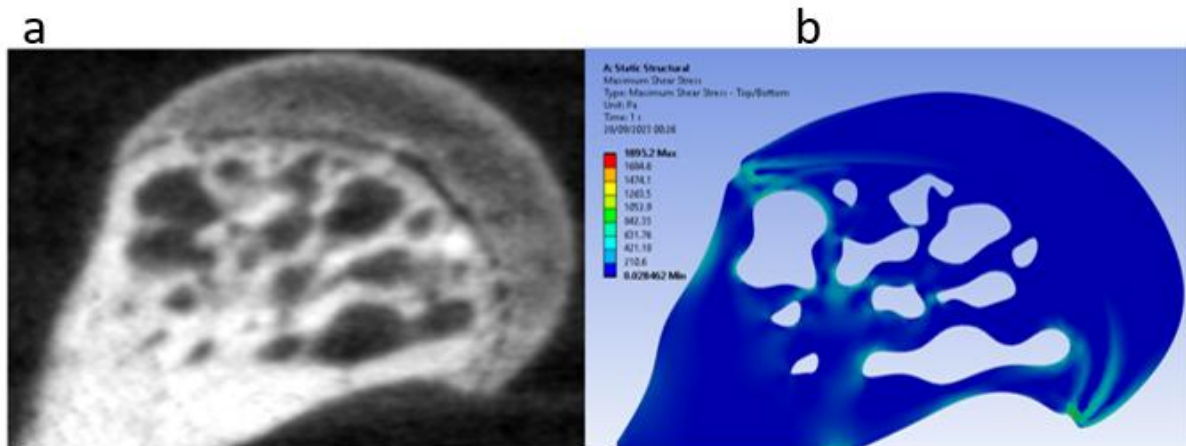


Figure 6 – a) μ Ct scan in C57BL6 mice, used for validation b) Zones of high shear stress in the growth plate (ANSYS,2023).

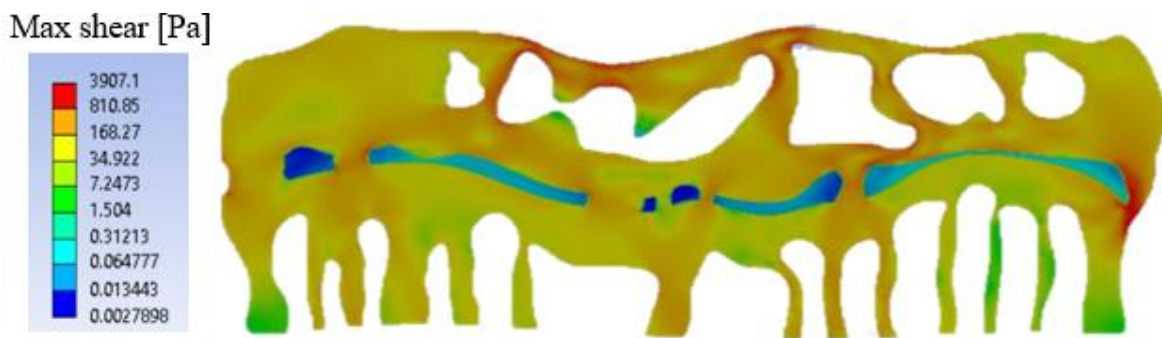


Figure 7 – Maximum shear stress distribution in the tibial plateau of a 2-month C57BL6 mice.

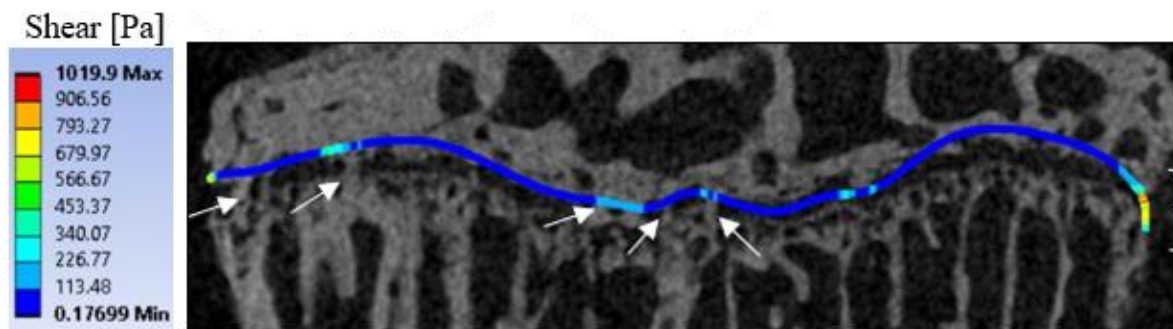


Figure 8 – Ossification points occurring at high shear stress points in the tibial plateau of a 2-month C57BL6 mice.

4 Discussion

These findings have important implications for the understanding of diseases affecting the growth plate. For instance, conditions like congenital pseudarthrosis, characterized by impaired bone healing, have been linked to poor trabecular patterns within the growth plate, in conjunction with SCFE, LCPD, and HD. Moreover, the proposed model offers a means to predict changes in bone development under abnormal loading conditions, such as hip dysplasia.

The investigation of trabecular patterns in the vicinity of the growth plate with a dynamic model presents an opportunity to identify early disease markers and potentially devise more effective treatment strategies for patients. Furthermore, a better understanding of trabecular patterns during healthy growth plate development provides insights into the optimal mechanical environment for bone growth. For instance, this knowledge could empower clinicians to innovate surgical techniques or design physical therapy protocols aimed at stimulating bone growth and facilitating healing in patients grappling with growth plate disorders. Subsequent studies are needed to yield insights into the precise mechanical conditions conducive to optimal bone growth and healing.

5 Conclusions

This work introduces a novel model to identify the morphological changes occurring in the growth plate during development. It accomplishes this by explicitly considering the influence of neighboring trabecular patterns while incorporating a bone remodeling scheme. The model output has been compared with clinical data and μ -ct scans derived from human and murine specimens. The comparison permits the quantification of changes in curvature within the epiphyseal plate and variations in local density. Furthermore, the model accurately reproduces the formation of ossification bridges, particularly in regions subjected to high shear stress, aligning closely with observations from μ -ct scans.

6 References

- [1] Moncayo et al. Morphological Changes of Physeal Cartilage and Secondary Ossification Centres in the Developing Femur of the House Mouse (*Mus Musculus*): A Micro-CT Based Study, *Journal of Veterinary Medicine Series C: Anatomia Histologia Embryologia*, 117-124, 2019.
- [2] Wilkinson et al. The Genetic Epidemiology of Joint Shape and the Development of Osteoarthritis, *Calcified Tissue International*, 257-276, 2021.
- [3] Vincent et al. The Morphogenesis of Porcine Femoral Head Mammillary Processes: A Structural Mechanism of Biomechanical Stability, 265-283, 2022.

- [4] Kandzierski et al. Shape of Growth Plate of Proximal Femur in Children and Its Significance in the Aetiology of Slipped Capital Femoral Epiphysis, *International Orthopaedics*, 2513-2520, 2012.
- [5] Nackenhorst. Numerical Simulation of Stress Stimulated Bone Remodeling, *Technische Mechanik*, 31-40, 1997.
- [6] Garzón et al. Comparative Analysis of Numerical Integration Schemes of Density Equation for a Computational Model of Bone Remodelling, *Computer Methods in Biomechanics and Biomedical Engineering*, 1189-1196, 2012.
- [7] Carter and Wong. Modelling Cartilage Mechanobiology, *Philosophical Transactions of the Royal Society B: Biological Sciences*, 1461-1471, 2003.
- [8] Quexada et al. Influence of Growth Plate Morphology on Bone Trabecular Groups, a Framework Computational Approach, 2023.
- [9] Uribe et al. Culturing and Measuring Fetal and Newborn Murine Long Bones, 1-9, 2019.
- [10] N F Krember Comparative Patterns of Cell Division in Epiphyseal Cartilage Plates in the Rabbit, 185-190, 1985.
- [11] Villemure et al. Growth Plate Mechanics and Mechanobiology. A Survey of Present Understanding, NIH Public access, 1793-1803, 2010.
- [12] Wong et al. A Theoretical Model of Endochondral Ossification and Bone Architectural Construction in Long Bone Ontogeny, *Anatomy and Embryology*, 523-532, 1990.
- [13] Belinha et al. Bone Tissue Remodelling Analysis Considering a Radial Point Interpolator Meshless Method, *Engineering Analysis with Boundary Elements*, 1660-1670, 2012.