SIMULATION BASED APPLICATION FOR OSTEOSYNTHESIS BY ELECTRO-OSMOSIS

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Abstract: - The bone tissue is in permanent remodeling. It adapts to the biomechanical requests by building bone tissue in the zones with strong loadings and by destroying it in the zones with weak loadings. This phenomenon is particularly well observed for example for the astronauts at the time of their missions in space when the quality of their bone tissue decreases in reason of the absence of loading [1]. Thus, thanks to these regenerative properties, when a bone is fractured, the realignment and the maintenance of the member are generally enough to generate new tissue. It's the process of osteogenesis. Many research teams studied the stimuli which can induce the bony remodeling: first of all, the mechanical stimuli related to the osseous matrix, the piezoelectric phenomena caused by collagen, the micro stresses generating the microscopic cracks; then, the movements of the interstitial fluid, which are induced by the mechanical stimuli. The idea that the fluid plays an important role in the bony remodeling seems to be accepted by the scientific community. Indeed, a few studies showed that the activity of the osseous cells varies considerably according to the fluid flow inside the osseous matrix [3]. In our previous studies [11, 12] one had studied the mechanism of the bony mechanotransduction, i.e. the way in which the cells receive the various stimuli and react, by building or destroying the bone tissue. The objective of this new study is a natural continuation of our previous works, by trying to determine in a numerical way if the induced consequences by the phenomenon of electrosmosis in the cylindrical unit structure of the bone which is the osteon, are able to stimulate the osteogenesis.

Key-Words: - bone remodeling, electro-osmosis , osteogenesis, numerical simulation, bone cells

1 Introduction

When a bone is fractured, the realignment and the maintenance of the member are generally enough to generate new tissue. It's the process of osteogenesis. This last covers the deficit due to the fracture and restores the structure of the bone and its functionality. But in some cases, this natural process of auto reparation is insufficient. On a fracture out of ten, mechanical or biological problems prevent this auto reparation after a fracture [2].In this case, the bone rebuilding must be assisted to rebuild functional skeletal tissues, equipped with good biological and mechanical properties. For doing this, the physicochemical constraints inducing the rebuilding of the bone must be well-known.

Firstly, a recall of anatomy concerning the bony structure will be carried out. Secondary, we will define the phenomenon of electrosmosis and the mathematical models allowing quantifying it. Then we will apply a model of Gouy-Chapman to our study and we will conclude on the impact of the electro osmosis on the bony remodeling.

2 Structure of the bone

The bones are composed of osteocytes cells surrounded by a mineral extracellular matrix with an organic part (the collagen fiber) and a mineral part (hydroxyapatite crystals). The human skeleton consists of three types of different bones, the flat bones, the short bones and the long bones. This study concerns the long bones and the compact bone remodeling.

The long bone is made up of three parts: a central part, the diaphyse, located between the two extremities of the bone and the epiphyses. A zone of transition between the epiphyse and the diaphyse can also be defined, it's the metaphyse [2]. The diaphyse of the long bones consists of compact bone tissue, contrary to the epiphyses and the metaphyses which consist of spongy bone tissue.

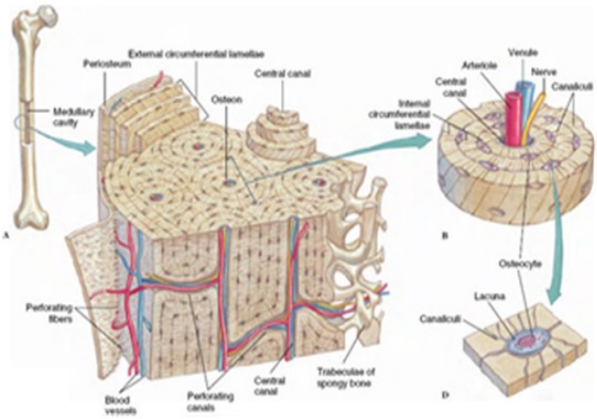
2.1 Macroscopic structure of the compact bone tissue

At a macroscopic scale, the compact bone tissue presents an organized architecture, made up of unit structures, called osteons. These osteons are cylindrical structures directed roughly in the same direction as the principal constraint which is exerted on the skeletal part. They are center crossed by the

Haversian channels. The Volkmann channels, located in transverse plans, connect the Haversian channels between them. This canal system allows the propagation of the movements of fluid from an area of the bone to the other when this last one is loaded mechanically.
The diameter of the osteons is about a few hundreds of micrometers. The Haversian channels have diameters of about 40-100 µm [4]. The space between two osteons is called interstitial system. The interface between osteons and interstitial system is called the cement line and has a thickness of approximately 1-5 µm [5].

2.2 Mesoscopic structure of the compact bone tissue

At mesoscopic scale (osteonale scale), the osteon is made of concentric lamellae, formed by mineralized collagen fibers. These lamellae contain osseous cells called osteocytes. These cells occupy the pores called lacunae and are connected by dendrites which are prolonged through some fine canaliculae. The osteocytes and their prolongations bathe in an interstitial fluid. The canaliculae leave the Haversian channel and move in a radial direction towards the end of the osteon without however reaching it. The lacunae are ellipsoidal cavities of 10-30 µm in diameter. The diameter of the canaliculae is about 0,1 µm [5].



Structure of compact bone tissue

2.3 Microscopic structure of the compact bone tissue

At the microscopic scale (lamellar scale), the lamella is regarded as a composite medium, the fibers being the collagen entities and the matrix being a medium made of hydroxyapatite crystals and fluid.

2.4 The remodeling of the compact bone tissue

The permanently renewal of the osseous matrix is carried out thanks to the balance between the action of two types of cells: the osteoblasts and the osteoclasts. The osteoblasts synthesize the osseous matrix while the osteoclasts eliminate growing old bone tissues under the control of a complex network of interactions between the osseous cells, the hormones, the growth factors, various physicochemical constraints related to the environment of the bone.
The bony remodeling is a cyclic process of about four months for an adult. A functional unit of remodeling realizes the formation of a structural unit (the osteon), by destroying and rebuilding the bone tissue according to six phases (see [6] for details): 1) the activation phase; 2) the resorption phase; 3) the inversion; 4) the formation; 5) the mineralization phase and 6) the quiescence phase.

3 Methods

This study was carried out at the macroscopic scale of compact bone tissue, at the osteonal scale. Inside this structure the osteocytes are bathing in the interstitial fluid. The movements of this fluid are suspected of ensuring the transmission of the macroscopic mechanical stimuli at the cellular scale by the means of the interactions between the fluid and the osteocytes, thus guaranteeing the mechano-transduction of the bony adaptation.
It should be noted that an osteon is hollow when it is in the stage of inversion and formation of the bony remodeling. Thus the study is carried out at the time of these two stages.

3.1 Modeling of an osteonal volume

A complete osteon is idealized by a hollow cylinder. The geometry is axisymmetric. The central hole models the Haversian channel. The diameter varies between 150 to 300 µm [5]. The height of the osteon corresponds to 1 µm.

3.1.1 Modeling of the liquid phase of an osteon

The Haversian channel is the “feeder” channel of the bone. It includes the blood capillaries and the related nerves. It is him which provides the fluid in osteon. Within the Haversian channel, the osmotic phenomenon occurs. Thus, there are two ways of modeling the liquid phase of osteons. Some consider that the composition of plasma is equivalent to that of the interstitial liquid. Other considers that the

composition of the interstitial liquid is not equivalent to that of plasma because it is richer in Cl^- ions and less rich in Na^+ ions. The following data will thus be taken into account in these two cases: Cl^-: 3650 mg for L (3898 mg for L); $PO4^{3-}$: 95-106 mg for L; CO_3H^- : 1650 mg for L; Na^+: 3300 mg for L (3067 mg for L); K^+: 180 mg for L; Ca^{++}: 100 mg for L; Mg^{++}: 18 mg for L; Cu^{++}: 1.2 mg for L; Fe^{+++}: 1 mg for L; Zn^{++}: 3 mg for L.

3.1.2 Modeling of the solid phase of an osteon

The study is placed in the case when the osteon is void, i.e. it has just undergone a resorption by osteoclasts. In this case the solid phase of the osteon corresponds to the cement line which is specific to each osteon. It consists of hydroxyapatite and is charged negatively by the negative ions of the liquid phase.

3.2 Electro kinetic phenomena

The osteon is a saturated and deformable porous environment. It consists of 3 phases: the solid phase represented by the cement line, the liquid phase represented by the interstitial liquid or plasma and the "in vivo" phase which corresponds to the bony cells (the osteoblasts cells, the osteoclasts and osteocytes) [6, 7, 8]. It is to be noted that in this study the cellular phase is integrated into the solid phase even if exchanges between fluid and cells may occur.

The conditions allowing the implementation of electro kinetic phenomena are thus present since when an ionic solution and a solid one are in contact, certain electro kinetic phenomena occur. They are four of them: electro-osmosis, flow potential, the electrophoresis and the potential of sedimentation.

This study concerns only the electro-osmosis phenomenon. The electro-osmosis is defined as being the actuation of a liquid through a porous environment when it is subjected to an electric field.

3.2.1 Modeling the electro-osmosis

Various theories were developed to describe the phenomenon of electro-osmosis and to quantify the electric potential which it generates. The most used theory is the theory of the "double layer". This is a model describing the variation of the electric potential on the surface panels.

The solid phase of the osteon is negatively charged by the negative ions of the liquid phase. The solid attracts by electrostatic forces, the cations which are in the liquid phase. The cations thus have a larger concentration close to the wall and try to diffuse because the thermal agitation tends to harmonize the concentrations. They are restricted in this diffusion by the electric field created on the surface of the solid. The two actions are counterbalanced in order to create distributions of ions in equilibrium [9].

The reverse phenomenon occurs for the anions, whose concentration is decreased close to the wall. The charged surface and the adjacent part in which the load is distributed are called double diffuse layer.

The theory of the double layer interprets the electro-osmotic phenomenon in the following way. During the application of an electric field on a porous environment negatively charged, the loads of the layer move in a direction which depends on their sign and on the direction of the electric field, they involve the liquid thanks to viscosity forces. Thus, there is no electric action on the neutral layer but this one is pulled up by viscosity by the double diffuse layer. It should be noted that in this layer are the negative and positive ions of the liquid phase of osteons. Thus, negative ions can circulate in the osseous matrix.

The theory of the double layer calls upon various models such as: the Helmhotz-Perrin model, the Gouy-Chapman model and the Stern and Grahame model. This study is based on the model of Gouy-Chapman since it takes into account the forces of thermal agitation inducing an ionic balance [10]. This aspect in the human body cannot be neglected.

3.2.2 Application of the Gouy-Chapman model

The model of Gouy-Chapman is an application of theory of the double layer described previously. In this model, one considers the ions as concentrated loadings, from here follows the concept of double diffuse layer.

This model is described entirely by two equations, the Poisson's equation and the equation of Boltzmann [9]. The Poisson's equation (1) establishes the relation between the potential difference between the osseous wall and the plasma contained in the center of the osteon, and the volume density of loads contained in the liquid.

$$\varphi = -\frac{\sum \rho i}{\epsilon} \qquad (1)$$

where φ is the electric potential (in Volts), ρ is the volume density of loads (in C m^{-3}) and ϵ is the dielectric permittivity of the medium (in F m^{-1}).

$$\epsilon = \epsilon_0 * \epsilon_{plasma} = 4.69272 * 10^{-8}\ F.m^{-1}$$

The volume density of loads for each ion can be calculated by the means of the following relation:

$$\rho_i = e*Na*v_i*n_i \qquad (2)$$

where *e* is the elementary charge of an electron ($1.602*10^{-19}$ C), v_i the valence of the ion *i* et n_i the concentration of ion *i;* Na is the Avogadro number: $6.023*10^{23}$.
Thanks to these two formulas, it is possible to calculate the electric potential of the solid phase φ^S corresponding to the potential of the negative ions of plasma or interstitial liquid and the electric potential of plasma and interstitial liquid φ^L.

$$\varphi_0 = \varphi(s) - \varphi(L) \qquad (3)$$

The Boltzmann equation (2) makes possible to establish the expression of the concentration volume of load according to the potential. This equation makes possible to take into account the influence of the temperature, so the thermal agitation. Thus, we have:

$$\varphi(x) = \varphi_0 \exp(-Kx) \qquad (4)$$

with $K = 1/l_d = F\sqrt{(2C/\varepsilon RT)}$, l_d being the length of debye. It translates the space extent of the fall of potential between the solid phase and the liquid phase; C corresponds to the ion concentration of the liquid phase; F is the Faraday constant which is equal to $9.65*10^{-4}$ C.mol^{-1}.
The application of this model requires the quantity of all the ions contained in the liquid phase of the osteon. Initially, we have at our disposal their mass concentration in gram; we must thus deduce the quantity of matter for each ion.
For example, if the intracellular concentration in chloride ions is of 0.1030 mol, the quantity of ions available in such a volume is of:
$0.1030 \times 7{,}85*10^{-16} = 8{,}09\ 10^{-17}$ mol of ions
Knowing that the diameter of an osteon varies between 150 and 300 µm we made this study for the following diameters: 150, 200, 250 and 300 µm.
Thanks to the equation (2), we can deduce the density of volume of charge for each ion: Cl^- : -1.7556E^{-07} C m^3; $PO4^{3-}$: -5.3862E^{-09} C m^3; Na^+ : 9.62834E^{-08} C m^3; K^+ : 8.06757E^{-09} C m^3; Ca^{++} : 8.5042E^{-09} C m^3 ; Mg^{++} : 2.6664E^{-09} C m^3 ; Cu^{++} : 6.44444E^{-11} C m^3 ; Fe^{+++} : 9.16716E^{-11} C m^3; ; Zn^{++} : 1.5643E^{-10} C m^3;
In order to obtain the distribution of the potentials between the cement line and the liquid phase of the osteon, it is initially necessary to calculate the potential φ_0. This potential corresponds to the difference of potential between the solid phase and the liquid phase of the osteon. We thus used the equation (1) in order to calculate these two potentials. Knowing that the solid phase of the bone is negatively charged, only the negative ions were taken into account. We thus obtain the following values: potential of the liquid phase (in V): 2.119080274; potential of the solid phase (in V): 4.58437805 and φ_0 (in V): 2.465297776.
It is enough now to determine K:

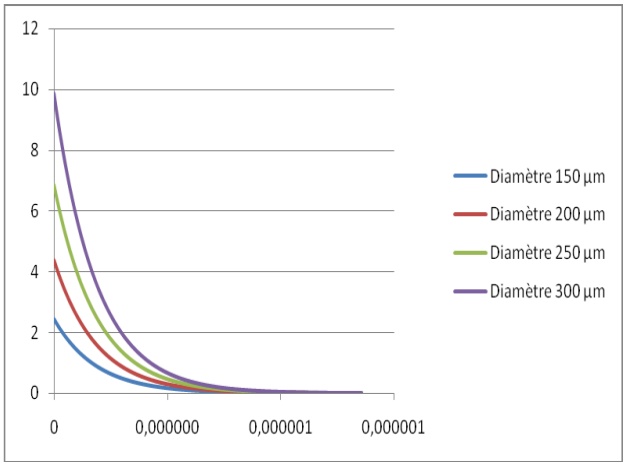
K ($1/l_d$)	5381022,731
l_d (length of debye)	1,85838E^{-07}

We thus have now all the elements to use the formula (4). Here are the first values we obtained:

x	φ(x)
0	2.465297776
0.000000005	2.399853007
0.00000001	2.33614556
0.000000015	2.274129316
0.00000002	2.21375938
0.000000025	2.154992048
0.00000003	2.097784777
0.000000035	2.042096153
0.00000004	1.987885861
0.000000045	1.935114657
0.00000005	1.883744338
0.000000055	1.833737716

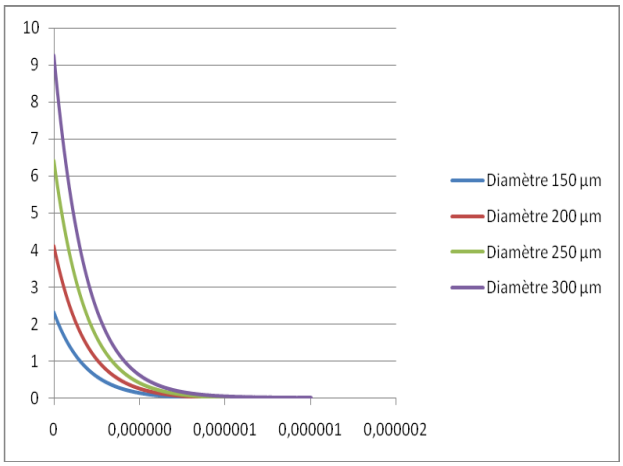
3.3 Results and Discussion

We realized the numerical calculus for plasma, the interstitial liquid and for some different diameters of osteon. Here they are:



φ(x) of plasma according to various diameters of osteon

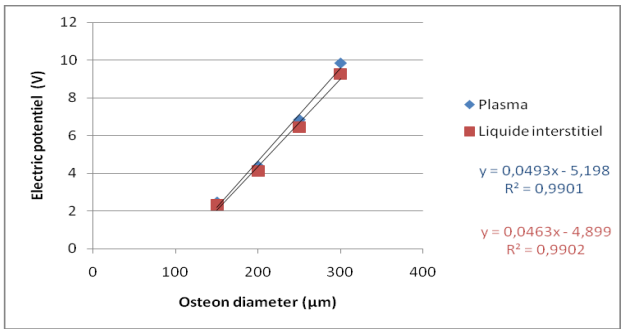
φ(x) of interstitial liquid according to various diameters of osteon



φ(x) of interstitial liquid according to various diameters of osteon

Evolution of the electric potential according to the diameter of osteon

In this study, we chose to work with two different liquid phases, which are plasma and the interstitial liquid. For the same diameter of osteon, so for the same volume, we obtain a potential φ_0 of the diffuse layer of 2,47 V for the plasma and 2,31 V for the interstitial liquid. Since the interstitial liquid presents a lower quantity of ions than plasma, it thus appears coherent that its electric potential is lower than that of plasma. However, this difference is not consequent (approximately 0,16 V), but on a cellular scale it can be at the origin of particular cellular behaviors. Thus, consider that the interstitial liquid can be substituted for plasma is not judicious, mostly when we place ourselves on a cellular scale. As an example, a neuron (nervous cell) is sensitive to potentials of order of the millivolt.



The evolution of the electric potential according to the diameter of osteon follows a linear progression, for plasma and the interstitial liquid. There is always a small difference between the electric potentials of plasma and the interstitial liquid. We noticed that this variation is constant.

4 Conclusion

Through this study, we could note that the phenomenon of electro-osmosis is susceptible to play an important role in the bone remodeling. Indeed, this phenomenon is at the origin of electric potentials being able to vary between 2,31 V and 9,26 V. These potentials come from the flow of fluids made up of ions. They are generally induced by the movements of the body and the external forces such as gravity. They can however be affected by growth factors.

The bony cells are stimulated by these potentials; it should be noted that the cells close to the cement line will be more solicitated than those being near the Haversian channel. It is obvious that according to the structural scale of the bone selected for the study, the potentials may change since we use other specimen as a model. It would be thus relevant that later studies try out the electro kinetic phenomena according to the various scales of the bone, aiming to justify the choice of the scale. Thus, a better knowledge of the electro kinetic phenomena on the various scales, would make possible to effectively stimulate the bony remodeling. It would be then possible to propose alternative treatments, less invasive than those existing, for the patients suffering from problems of bone reconstruction.

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References:

[1] E.R .Morey and D.J Baylink, Inhibition of bone formation during space fight, *Science*, Vol. 201, No. 4361, 1978, pp. 1138-1141

[2] INSERM. Réparer l'os : bio-ingénierie de l'os, http://www.inserm.fr/thematiques/technologies-pour-la-sante/dossiers-dinformation /biomateriaux /reparer -l-os-bio-ingenierie-de-l-os

[3] K.M Reich and J.A Frangos 1991, Effect of flow on prostaglandine 2 inositol triphosphate levels in osteoblasts, *Am J.Physiol,* No. 261, 1991, pp. C428-C423

[4] Thibault Lemaire and Salah Naïli, Approche multi-échelle des phénomènes couplés intervenant dans la mécanotransduction du remodelage osseux, *Talk to the 18th Congrès Français de Mécanique*, France, 2007

[5] Fabien Borocin, Thibault Lemaire and Salah Naili, Modélisation poroélastique de l'os cortical isotrope transverse : comparaison entre ostéons sain et pathologique, *Talk to the 18th Congrès Français de Mécanique*, France, 2007

[6] T. Lemaire, S. Naili, Stimuli physiques du remodelage osseux (Physical stimuli of bone remodelling), in *Reconstruction osseuse et cutanée: Biomécanique et Techniques de l'Ingénieur*, Eds. Sauramps Medical, Montpellier-France, 2008, pp. 57-71

[7] H. Hermann, JF Cier, *Le plasma et le liquide interstitiel. Précis de physiologie,* Masson and Cie , 1989

[8] P.Page, J. Curtis, Morley C, *Integrated Pharmacology,* First edition, Mosby International, 1997

[9] J.Bocus, *Electro-osmotic transport in deformable porous media. Application to Agar gel,* PhD thesis, Université MonpelierII, 2005

[10] Fabien Miomandre, SaïdSadki, PierreAudebert, RachelMéallet-Renault, *Des concepts aux applications. Électrochimie*, 2e édition, Dunod, 2011

[11] M. Racila and J.M. Crolet, SiNuPrOs : Mathematical Model of Human Cortical Bone, *Recent Advances in Mathematics and Computers in biology and chemistry*, ISBN: 978-960-474-062-8, ISSN: 1790-5125, WSEAS Press, 2009, pp. 53-58

[12] M.C. Stroe, J. M. Crolet, M. Racila, Mechanotransduction in cortical bone and the role of piezoelectricity: a numerical approach, *Computer Methods in Biomechanics and Biomedical Engineering* , Vol. 16, No. 2, 2013 pp. 119-129