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## Uncertainty quantification on a chemical poroelastic coupled problem: Mechanobiology of implant healing

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### Abstract

The fixation of a bone implant is related to the quality of tissue in the vicinity thereof. A numerical model is relevant to improve the understanding of mechanobiological events involved and to guide the implantation surgery. To build a robust model that integrates a large number of biomechanical parameters that are subject to variability, uncertainty propagation is analysed. In this work, a numerical model coupling of biochemistry and poroelasticity is proposed and it is applied to canine model. The model includes a nondimensionalization with control of the time and a stochastic modelling. The deterministic part of the model produces the bone density field, corresponding to the quantity of interest, at the end of the healing after several weeks. In particular, it takes into account the influence of external mechanical excitations on the healing process. To limit the costs of computing and development, the stochastic analysis is chosen by the non-intrusive method of probabilistic collocation with development of the polynomial chaos. The results obtained include the effect of coupling between the different sources of uncertainty and allow the influence of biochemical and mechanical parameters such as the applied displacement on the quality of the periprosthetic tissue healing to be quantified.

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**Keywords:** Uncertainty quantification ; probabilistic collocation method ; multiphysics interaction ; computational biomechanics ; implant fixation.

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### 1. Introduction

Orthopedic implants are currently one of the most used products in the implantable medical devices field. The clinical longevity of these implants is primarily determined by the quality of their fixation to the surrounding bone. Moreover, the clinical condition of the patient, the surgical technique and coupled mechanical and biochemical factors have a crucial influence on the bone growth in the early post-operative period, for example, see [1].

A comparative study has been made between ex-vivo data from the healing of a canine implant [2] and numerical models [3]. The biological tissue can be modelled by a multiphase reactive medium with poromechanical and cell

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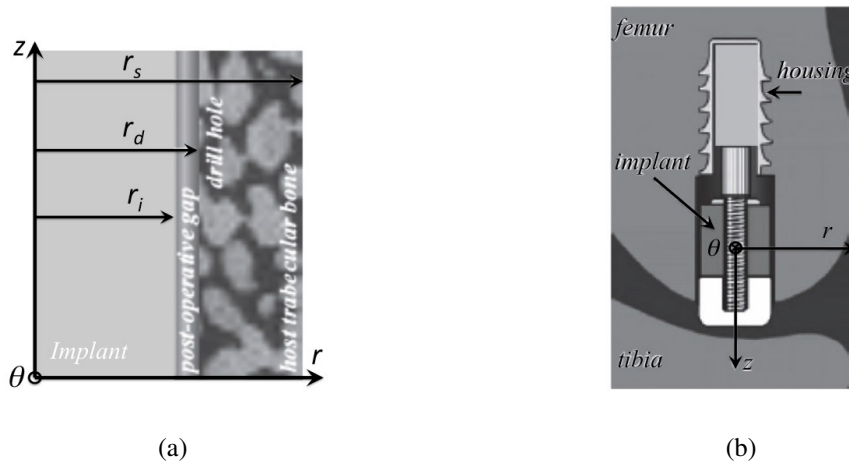


Fig. 1. Canine implant: (a) axisymmetric model, (b) implant diagram

biology characteristics. Osteoblast cells migration, growth factors diffusion and bone deposit are considered [3]. Mechanical factors coupled with the biochemical factors were studied in [4] using a poroelastic biochemical model.

The complex mechano-biochemical environment induces uncertainties that need to be predicted by considering non linear coupling effects in the multiphysics equations. These influences have been studied on the healing of a canine implant modelled by the biochemical porous medium model developed in [3], for several random individual biochemical factors [5,6].

The heterogeneity of the periprosthetic tissue healing may be revealed by considering the porous medium as deformable [4]. This study aims to predict the bone healing process evolution induced by the variability of a mechanical and biochemical factors. A probabilistic collocation method based on the polynomial chaos expansion is used [7–9]. Illustrations on the bone formation during the post-operative period are presented.

## 2. Implant poroelastic problem

A poroelastic model [4] consists of a multi phasic porous model which involves the solid osseous fraction, the extracellular fluid phase, the osteoblastic cellular phase responsible from the bone formation and the growth factor phase promoting the cellular activity, and the elasticity of the skeleton of the porous medium. In this work, a daily activity is considered by applying a prescribed displacement as a function of time.

The set of conservation laws of the problem are

$$\frac{\partial}{\partial t} \phi^s = r^s, \quad (1)$$

$$\frac{\partial}{\partial t} [(1 - \phi^s)C^c] = \text{div} \mathbf{q}^c + r^c, \quad (2)$$

$$\frac{\partial}{\partial t} [(1 - \phi^s)C^M] = \text{div} \mathbf{q}^M, \quad (3)$$

$$\text{div} \boldsymbol{\sigma} = \mathbf{0}, \quad (4)$$

$$\mathbf{q} = \text{div} \mathbf{w}^f, \quad (5)$$

where  $\phi^s$  is the solid fraction of new formed tissue,  $\mathbf{w}^f$  is the relative fluid flow rate and  $\boldsymbol{\sigma}$  is the stress of the porous medium.

$\mathbf{q}^c$ ,  $\mathbf{q}^M$ ,  $r^c$ ,  $r^s$ ,  $\boldsymbol{\sigma}$ ,  $\mathbf{q}$  and  $\mathbf{w}^f$  are given by the constitutive laws:

$$\mathbf{q}^c = (1 - \phi^s) \left( D^c \mathbf{grad} C^c - h^c \rho^s C^c \mathbf{grad} \phi^s - \chi^c C^c \mathbf{grad} C^M \right), \quad (6)$$

$$\text{and } \mathbf{q}^M = D^M (1 - \phi^s) \mathbf{grad} C^M + C^M \mathbf{q}^f \quad \text{are the two convective and diffusive equations,} \quad (7)$$

$$r^c = \alpha^s [(1 - \phi^s) C^c] [N^{cc} - (1 - \phi^s) C^c], \quad (8)$$

$$\text{and } r^s = \alpha^s [(1 - \phi^s) C^c] [(1 - \phi^s) C^M] \quad \text{are the two reactive equations,} \quad (9)$$

$$\boldsymbol{\sigma} = \mathbf{D}\boldsymbol{\epsilon} - b p \mathbf{I} \quad \text{is Hooke's law,} \quad (10)$$

$$\mathbf{q} = \frac{1}{Q} \dot{p} + b \text{tr}(\dot{\boldsymbol{\epsilon}}) - \dot{\phi}^s \quad \text{is the rate of fluid accumulation} \quad (11)$$

$$\text{and } \mathbf{w}^f = H \mathbf{Z} \quad \text{is Darcy's law.} \quad (12)$$

$\alpha^s$ ,  $h^c$ ,  $\chi^c$  are respectively the coefficients of osteoid synthesis, haptotactic migration and chemotactic migration, and are of uncertain value. The osteoblast cell proliferation is represented by its coefficient  $\alpha^c$ , its inhibition level  $N^{cc}$ , its concentration  $C^c$ , its flow rate  $\mathbf{q}^c$  and its diffusion factor  $D^c$ . Similarly,  $C^M$ ,  $\mathbf{q}^M$  and  $D^M$  are associated to the growth factor concentration. Density of the solid phase is denoted by  $\rho^s$ .  $\mathbf{D}$  represents Hooke's operator,  $\boldsymbol{\epsilon}$  is the strain of the porous medium,  $b$  is the Biot coefficient,  $p$  is the pore pressure and  $\mathbf{I}$  is the identity matrix.  $Q$  is the Biot modulus and  $\text{tr}(\bullet)$  is the trace operator. Finally,  $\mathbf{Z}$  is the pressure gradient given by  $\mathbf{Z} = \mathbf{grad} p$  and  $H$  is the permeability factor.

### 3. Stochastic modelling

In this work, the uncertainties are modelled by the stochastic response surface method [7–9]. This probabilistic collocation method calculates the response as an expansion of stochastic orthogonal polynomials associated to the probability law of the random inputs. As shown in [5], variation in the values of some biochemical factors  $\chi^c$ ,  $h^c$  and  $\alpha^s$  change the implant healing. The problem considered is axisymmetric as shown in Fig. 1 and verifies the plane strains assumption. A radial displacement  $u_a$  is applied on the implant and is considered as random. All inputs follow the uniform probability distribution and are expanded in random variables  $\boldsymbol{\xi}$  using the Karhunen Loeve expansion. Three problems of two random variables each ( $\chi^c$  and  $u^a$ ;  $h^c$  and  $u^a$ ;  $\alpha^s$  and  $u^a$ ) are then considered and compared to the analysis in [5]. The random output is the solid fraction  $\phi^s(r, \boldsymbol{\xi})$ , with  $\boldsymbol{\xi} = \{\xi_1, \xi_2\}$  the random vector.  $\phi^s(r, \boldsymbol{\xi})$  is expanded in a truncated summation of polynomial chaoses  $\Psi_i$  as follows

$$\phi^s(r, \boldsymbol{\xi}) = \sum_{i=0}^N \phi_i^s(r) \Psi_i(\boldsymbol{\xi}) \quad (13)$$

where  $\phi_i^s$  are deterministic coefficients and  $N$  is the order of truncation equal to  $N = (n+p)!/n!/p! - 1$  with  $p$  the order of the polynomial chaos expansion.  $r$  is the radial coordinate of the polar frame (Fig. 1). The unknown coefficients  $\phi_i^s$  of the expansion are obtained from the minimization of

$$\min_{\phi_i^s(r)} \sum_{k=0}^{N_\xi} \left[ \phi^s(r, \boldsymbol{\xi}_k) - \sum_{i=0}^{N_\phi} \phi_i^s(r) \Psi_i(\boldsymbol{\xi}_k) \right]^2 \quad (14)$$

The collocation points  $\boldsymbol{\xi}_k$  are chosen as roots of the  $(N+1)^{\text{th}}$  order polynomials [7]. Among all the linear combinations of the roots, the collocation points are chosen in order to capture the solution in the regions of high probability [8,9].

### 4. Numerical results

The results of the bone healing process are computed after 8 weeks. The radial displacement  $u^a$  is a sinusoidal function of period  $T = 24$  hours and of magnitude  $a$  [4]. It is applied at  $r = r_i$  shown in Fig. 1. Common values for the healing patterns are  $N^{cc} = 1000 \text{ cell/mm}^3$ ,  $\alpha^c = 1.9 \times 10^{-10} \text{ mm}^3/\text{cell.s}$ ,  $D^c = 2.5 \times 10^7 \text{ mm}^2/\text{s}$ ,  $D^M = 4.8 \times 10^{-6} \text{ mm}^2/\text{s}$ ,  $\rho^s = 2.57 \times 10^{-6} \text{ kg/mm}^3$ , and geometrical parameters  $\delta_d = 0.1 \text{ mm}$ ,  $r_i = 3.25 \text{ mm}$ ,  $r_d = 4.1 \text{ mm}$ ,  $r_s = 7$

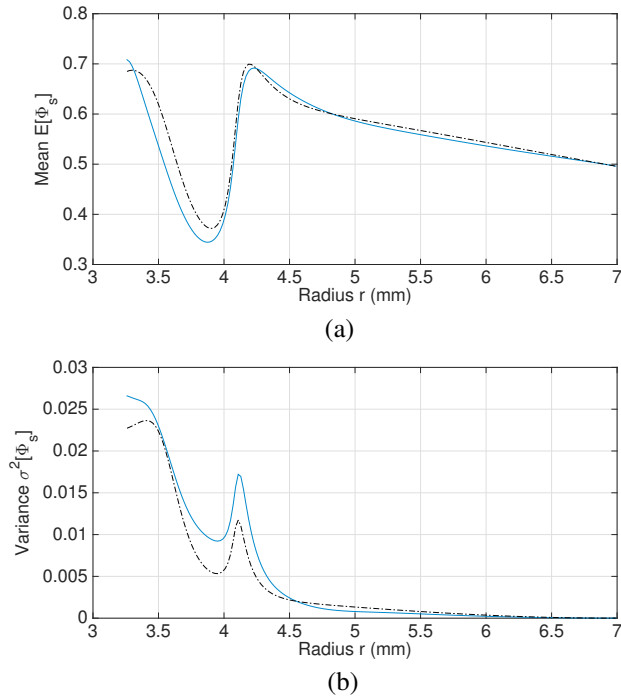


Fig. 2. Random solid fraction as a function of the radius when  $\alpha^s$  and displacement  $a$  are random variables. (a) Mean ; (b) Variance. Poroelastic model (blue solid line), Rigid model (black dashed dotted lines)

mm (Fig. 1). The magnitude  $a$  and the three biochemical factors  $\chi^c$ ,  $h^c$  and  $\alpha^s$  follow a uniform law within the ranges given in Table 1 [5]. The output  $\phi^s$  is expanded in terms of orthogonal Legendre polynomials. Convergence in all computations is obtained with a third order ( $p = 3$ ) of the expansion, and then 16 collocation points for two random parameters.

It was shown in [5] that variations of three biochemical factors had a different influence on the healing between the implant surface  $r_i$  and drill hole  $r_d$ . The most influenceable parameter is the osteoid synthesis  $\alpha^s$  with a variation of the healing at both the implant surface  $r_i$  and drill hole  $r_d$ . The chemotactic coefficient  $\chi^c$  had also a significant impact but mainly influenced the implant surface which determines the tissue formation. Finally, the haptotactic coefficient  $h^c$  responsible for the homogeneity of the solid fraction into the post-operative gap showed a light effect.

Figs. 2 to 4 present the random solid fraction given by its mean and variance, Results are presented for both the poroelastic model with a random displacement presented here and a rigid porous model presented previously in [5]. For each biochemical factor, the presence of an applied displacement slightly decreases the healing between the implant surface  $r_i$  and drill hole  $r_d$  as shown by the mean of the solid fraction in Figs. 2(a) to 4(a). The variance of the solid fraction obtained by the poroelastic model follow similar trends as for the rigid case but are increased in the gap  $r_i - r_d$ , yielding the prediction of the healing harder to define in this region.

Table 1. Random parameters of the numerical model

Biochemical factors	
$\chi^c$ ( $\text{mm}^5 \cdot \text{ng}^{-1} \cdot \text{s}^{-1}$ )	$[1, 14.5] \times 10^{-5}$
$h^c$ ( $\text{mm}^5 \cdot \text{kg}^{-1} \cdot \text{s}^{-1}$ )	$[4, 80] \times 10^{-2}$
$\alpha^s$ ( $\text{mm}^6 \cdot \text{cell}^{-1} \cdot \text{ng}^{-1} \cdot \text{s}^{-1}$ )	$[1, 5] \times 10^{-9}$
Displacement	
$a$ (mm)	$[0, 1.2]$

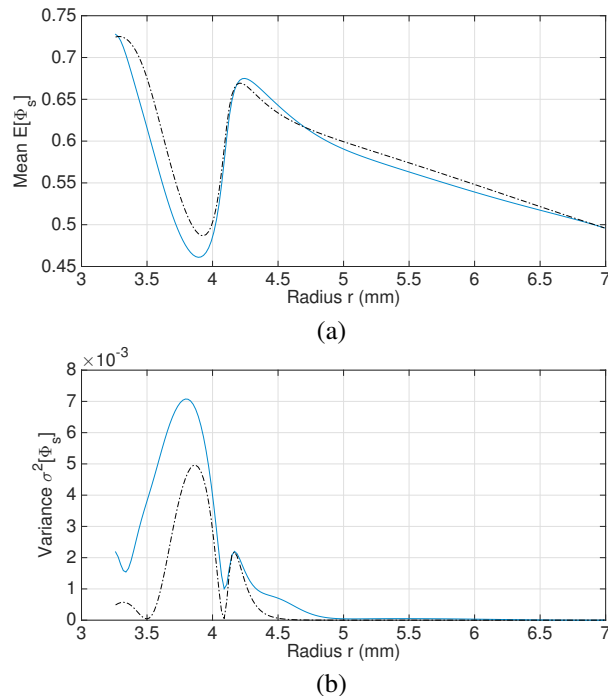


Fig. 3. Random solid fraction as a function of the radius when  $h^c$  and displacement  $a$  are random variables. (a) Mean ; (b) Variance. Poroelastic model (blue solid line), Rigid model (black dashed dotted lines)

## 5. Conclusions

This paper aims to integrate uncertainties on the mechanical aspect of the mechano-biochemico bone healing after the implantation surgery. A numerical model has been developed using an axisymmetric poroelastic biochemical medium model and a stochastic non intrusive method. The uncertain mechanical parameter representing the daily activity of the patient showed an increase of the uncertainty in a crucial gap radius responsible of the healing of the bone and also of the quality of the implant fixation.

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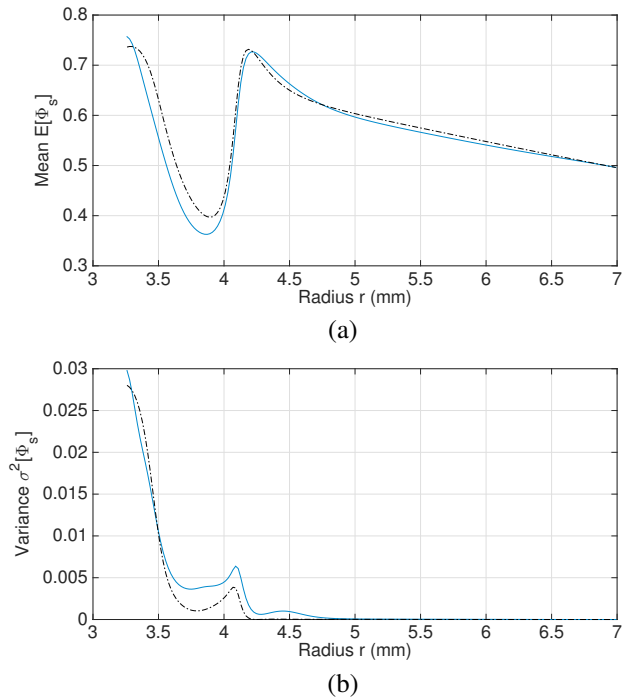


Fig. 4. Random solid fraction as a function of the radius when  $\chi^c$  and displacement  $a$  are random variables. (a) Mean ; (b) Variance. Poroelastic model (blue solid line), Rigid model (black dashed dotted lines)

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