

Nonlinear ultrasound: Potential of the cross-correlation method for osseointegration monitoring

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Abstract: Recently the concept of probing nonlinear elasticity at an interface prosthesis/bone has been proposed as a promising method to monitor the osseointegration/sealing of a prosthesis. However, the most suitable method to achieve this goal is a point of debate. To this purpose, two approaches termed the scaling subtraction method and the cross-correlation method are compared here. One nonlinear parameter derived from the cross-correlation method is as sensitive as a clinical device based on linear elasticity measurement. Further, this study shows that cross-correlation based methods are more sensitive than those based on subtraction/addition, such like pulse inversion and similar methods.

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The work described here is part of the long-term goal to implement new non-invasive methods to monitor bone prostheses sealing or osseointegration *in vivo* (dental implants, hip prostheses). Although the most widely used clinically, x-ray radiography suffers from low sensitivity,¹ limiting for instance its ability to detect early loosening of a prosthesis. This has led to much research based on elasticity measurements that do not ionize tissue.² Among these measurements and as detailed in Ref. 3, nonlinear elasticity could be of interest in providing information regarding contact integrity because the nonlinearity likely comes from frictional effects and/or clapping sources.

Several groups have attempted measurement of nonlinear parameters at an interface bone/hip prosthesis.^{4,5} These studies are promising but are primarily based on a single nonlinear method: the measurement of harmonic amplitudes in the frequency domain. Furthermore, most of these studies are only conducted for extreme cases of stability. Information over the entire osseointegration process, from the very loose to the well-secured case, would therefore be useful to advance our knowledge on the subject.

To this aim, two previous studies from our group were applied using simple experimental models and various experimental methods to probe nonlinear elasticity.^{3,6} A nonlinear resonant method,⁶ performed on a model made of two weakly damped materials, confirmed the greater sensitivity of the nonlinear response to the contact quality and demonstrated that a broad frequency band is useful to increase the sensitivity range. A more realistic interface composed of a dental implant and a bone phantom was then studied.³ Despite less favorable conditions to the presence of nonlinearity (strong attenuation and greater difference in elasticity between both materials in

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contact), a focusing technique based on time reversal provided the means for the extraction of a nonlinear parameter sensitive to the implant stability. Nevertheless, there existed drawbacks regarding this study,³ such as the manner of mimicking the osseointegration or the fact that the focusing technique requires substantial equipment.

In the following, we compare two promising methods for osseointegration monitoring, with the goal of ultimately applying one of them *in vivo*. These methods are promising because (i) they both require limited equipment to measure nonlinearity and are therefore suitable for *in vivo* measurements, (ii) they allow one to obtain the entire nonlinear response, (iii) they are suitable to highly damped media such as bone, and (iv) a large frequency band can be probed with both methods. Beyond this application, comparison of these two methods is informative for numerous different domains exploiting nonlinearities, such as non-destructive testing and contrast agents imaging.

The method used for mimicking osseointegration is described as follows. A sample of mock cortical bone [Short fiber filled epoxy sheet (28 mm × 25 mm × 10 mm) from Sawbones (Malmö, Sweden)] is used for the experiment [Fig. 1(a)]. The mock cortical bone has elastic, dissipative, and density properties similar to human cortical bone (anisotropy included). However, no information regarding the nonlinear elastic properties is given by the manufacturer. A 4.2-mm hole is drilled in the sample center and threaded with a dental implant [4.8 mm-diameter, SwissPlus tapered from Zimmer (Carlsbad, CA)]. The sample is then cut along the two dashed lines shown in Fig. 1(a). The two pieces are then bonded to a vice with cyanoacrylate. This cut avoids contact between the two pieces when the implant is placed in between. Thus tightening the vice primarily results in a more intimate contact between the mock bone and the implant. Two piezoceramics (PZT-5A, diameter 3 mm, thickness 2 mm, Fuji Ceramics, Tokyo, Japan) are bonded on the implant to excite the system and record the response.

A 240° rotation of the vice corresponding to a 1-mm displacement takes the sample from loose to well secured. Three hundred degrees is taken as a reference for a

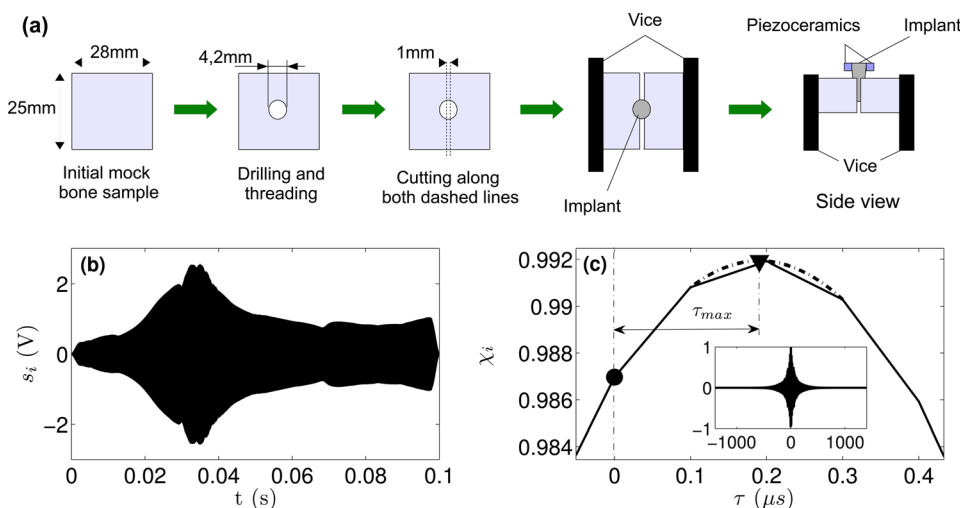


Fig. 1. (Color online) (a) Experimental setup and its preparation. (b) Typical signal recorded from the swept-sine excitation. The frequency linearly increases from 60 to 120 kHz in the signal. (c) Typical normalized cross-correlation function obtained for the CCM method. The circle and triangle correspond respectively to the inter-correlation level at $\tau = 0$ and to the maximum of intercorrelation. The time-shift τ_{max} is represented by the arrow. The three highest points of the intercorrelation function are interpolated with a parabolic function (dashed line), allowing one to obtain τ_{max} and χ_i^{max} with a better accuracy than the sample frequency and the vertical resolution of the acquisition card respectively.

well-secured implant. Measurements are then performed each 30° angular interval, with nine discrete steps for a complete procedure. This manner of monitoring allows one to change only the normal stress at the interface during the tightening. It is thus more realistic than a screw/plate-based system,³ which induces a unwanted vertical change between both materials due to the helicoid motion. Results are averaged over three procedures, while removing of the implant between each procedure.

A swept-sine source (60–120 kHz) is used in both ultrasonic methods for the excitation of one piezoceramic. This large frequency band is selected to maximize the stability range monitoring.⁶ This specific range is also chosen because it contains various modes of the implant.³

The first nonlinear ultrasonic method used is the scaling subtraction method (SSM).⁷ It consists of successively sending two pulses, one low amplitude A_{ref} assumed linear and one larger amplitude A_i assumed nonlinear. By rescaling both responses and computing the difference, the full nonlinearity is obtained. Then the elastic nonlinear energy Ω_i of this difference is extracted as follows:

$$\Omega_i = \frac{1}{T} \int_0^T \left[s_i(t) - \frac{A_i}{A_{ref}} s_{ref}(t) \right]^2 dt \quad (1)$$

where $s_{ref}(t)$, $s_i(t)$, and T refer, respectively, to the reference recorded signal corresponding to a low amplitude excitation, the recorded signal corresponding to a higher excitation amplitude, and the signal duration (100 ms). A typical recorded signal is displayed in Fig. 1(b).

The second method, the cross-correlation method (CCM), differs from SSM in the sense that the cross correlation of these two signals is taken rather than the difference. The method showed convincing results for the study of linear and nonlinear scattering regimes in granular media.^{8,9}

As shown in Fig. 1(c), three parameters are extracted from the CCM: (i) the intercorrelation amplitude for a 0-shift, (ii) the time-shift value τ_{max} corresponding to the maximum intercorrelation, and (iii) the value of this maximum. For a linear system, τ_{max} is zero and parameters (i) and (iii) have the same value. In a practical sense, parameters (i) and (iii) are obtained as follows:

$$\chi_i^0 = \chi_i(0) = \frac{C_{ref,i}(0)}{\sqrt{C_{i,i}(0)C_{ref,ref}(0)}}, \quad (2)$$

$$\chi_i^{\tau_{max}} = \chi_i(\tau_{max}) = \frac{C_{ref,i}(\tau_{max})}{\sqrt{C_{i,i}(0)C_{ref,ref}(0)}} \quad (3)$$

where $C_{ref,i}(\tau) = \int_0^T s_{ref}(t)s_i(t-\tau)dt$. Autocorrelations $C_{ref,ref}$ and $C_{i,i}$ used for both denominators normalize the two nonlinear parameters, making them independent of the energy.⁸ Thus parameters χ_i^0 and $\chi_i^{\tau_{max}}$ equal 1 if both signals match perfectly (linear system).

For both methods, a “zigzag” procedure¹⁰ is applied that consists in exciting the system at the low reference excitation amplitude (0.1 V) between each increasing amplitude (0.1–3 V). Using the low reference amplitude just preceding the i th amplitude to calculate SSM and CCM parameters provides the means to correct the potential slight environmental variations (temperature, humidity). It has been shown that this procedure increases accuracy by one order of magnitude.¹⁰ Further, one can also see that one order of magnitude in amplitude is used for these experiments (from 0.1 to 3 V), making nonlinear parameters relevant.

As shown in Fig. 1(b), the output amplitude is not constant over the frequency range. Thus we define the output energy of each signal as $\Lambda_i = (1/T) \int_0^T s_i^2(t)dt$ and the

four parameters previously defined (1 for SSM, 3 for CCM) are extracted for each excitation amplitude and represented as a function of Λ_i .

Results for both SSM and CCM are presented in Fig. 2. Figure 2(a) shows the evolution of the SSM parameter Ω versus the output energy Λ . We observe a decrease of Ω with tightening, meaning that the system becomes more linear. Similar results are obtained with CCM parameters in Figs. 2(b) to 2(d). Indeed, the temporal parameter τ_{max} decreases with tightening, while χ^0 and χ^{max} approach the value 1, corresponding to a linear case. Each trend in Figs. 2(a) to 2(d) is interpolated to obtain four nonlinear indicators independent of the excitation amplitude. Meaning four power functions $a(\Lambda - \Lambda_1)^b$ fit experimental data in Figs. 2(a) to 2(d). b is a constant for each parameter and equal to 1.7, 0.5, 0.5, and 0.4 for Ω , τ_{max} , χ^0 , and $\chi^{\tau_{max}}$ respectively. Figures 2(e) to 2(h) show the evolution of the four deduced nonlinear indicators a versus tightening, the sensitivity of which can be compared with any other method.

It is seen that a_Ω and $a_{\tau_{max}}$ decreases with tightening, while a_{χ^0} and $a_{\chi^{\tau_{max}}}$ increases. This observation confirms the sensitivity of all indicators to the quality of contact between both materials. Nevertheless, the extracted parameter from SSM (a_Ω) has larger error bars, meaning that CCM seems to be a more accurate tool than SSM to measure nonlinearities. Further, we observe that $a_{\tau_{max}}$ is sensitive until the last tightness step due to higher reproducibility, while sensitivity of a_Ω , a_{χ^0} , and $a_{\chi^{\tau_{max}}}$ is null for the last two or three steps.

The sensitivity of $a_{\tau_{max}}$ is compared in Fig. 3 with that of a clinical linear device measuring the frequency of the first bending mode of the implant² (RFA for resonance frequency analysis). An highest frequency is expected for optimal stability and this frequency is converted into an ISQ indicator (implant stability quotient) ranging from 0 (low stability) to 100 (high stability). Sixty five is given by the manufacturer as a minimal value for a reliable stability. -ISQ is plotted in Fig. 3 to get the same variation direction for both indicators. A very similar behavior is observed for both linear and nonlinear indicators as well as an equivalent sensitivity. This result is encouraging because we obtain the same sensitivity with CCM as that of a commercial device subject to a thorough optimization. Future developments and/or optimizations on CCM

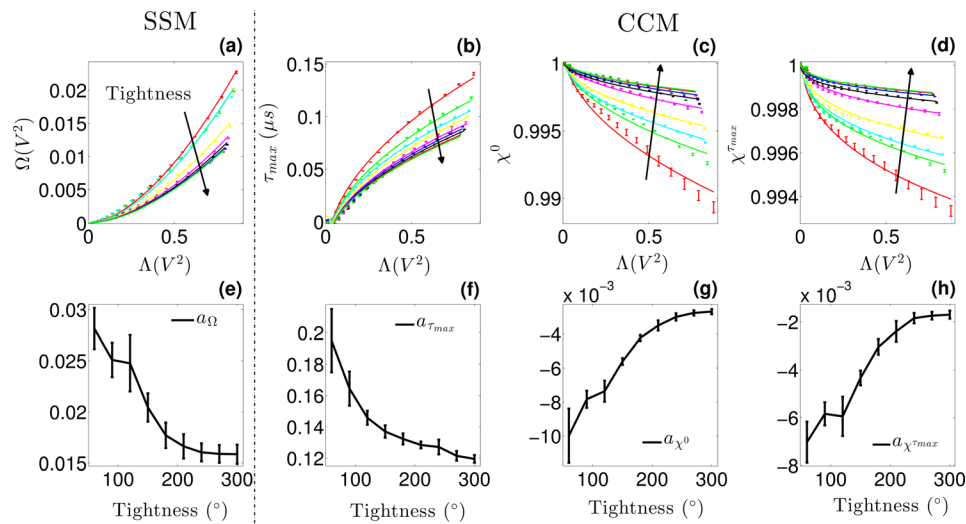


Fig. 2. (Color online) (a) to (d) Evolution of the four nonlinear parameters and associated interpolations versus output energy Λ for nine tightness levels. Interpolations are $a(\Lambda - \Lambda_1)^b$ with b equal to 1.7, 0.5, 0.5, and 0.4, respectively, for Ω , τ_{max} , χ^0 , and $\chi^{\tau_{max}}$. (e) to (h) Evolution of the four nonlinear indicators a extracted from these interpolations.

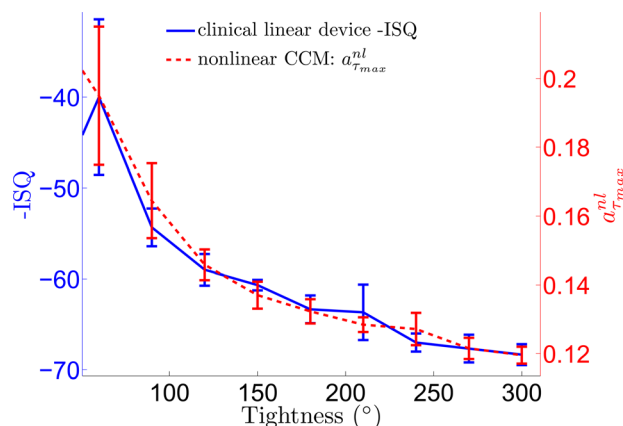


Fig. 3. (Color online) Sensitivity comparison of a linear device and the nonlinear indicator $a_{\tau_{max}}^{nl}$. A very similar evolution and sensitivity for both parameters can be observed.

could include the use of a still larger frequency band to probe different scales of the interface.

A short discussion on interpolations used in Figs. 2(a) to 2(d) follows. Coefficients b representing the curvature level of interpolation's functions are selected empirically to fit experimental data. In particular, it can be seen in Figs. 2(c) and 2(d) that the first two tightness steps are only roughly fit by these interpolations. However, even if the curvature changes slightly from one tightening step to the other, we arbitrarily choose to keep the parameter b constant all along the tightening steps to be able to compare a same parameter a .

Also we can compare the interpolations made here with the simplest nonlinear elastic models. It can be shown with a one-dimensional model in the forced regime,^{11,12} and under the assumption of a single mode in the frequency band, that a quadratic hysteretic model leads to a coefficient b equal to $\{2; 0.5; 1; 1\}$ for parameters $\{\Omega; \tau_{max}; \chi^0; \chi^{\tau_{max}}\}$, respectively. Also, cubic nonlinearity leads to the set $\{3; 1; 2; 2\}$. Experimental data leading to $\{1.7; 0.5; 0.5; 0.4\}$ are closer from the hysteretic model, and this may be expected because most experiments involving damaged materials and/or rough interfaces lead to this behavior. Differences observed can likely come from the fact that only one mode is considered in the model, ignoring possible coupling between modes.

One primary limitation of this study is the fact that the static stress at the interface is unknown during measurements. The tightening reproducibility is only controlled through the angular position of the vice. However, we assume that the static stress range is appropriate because stability levels given by the commercial linear device are similar to clinical values ($ISQ = 68 > 65$ for the last tightening steps in Fig. 3).

In this study, we compare two promising methods for osseointegration monitoring and based on nonlinear elasticity measurements. These two methods provide the means to obtain the entire nonlinear response over a large frequency band and both are found sensitive to the mimicking model used in this experiment. We also show that the parameter extracted from the cross-correlation method is as sensitive as a linear device already used clinically. These encouraging results will be carry on in the future with *in vitro* and *in vivo* measurements.

Finally, this study shows that beyond the scope of this application, cross-correlation based methods seem to be a more sensitive approach than methods based on addition/subtraction (pulse inversion and derived methods). This last class of methods is being widely used in non-destructive testing and/or contrast agents imaging; some improvements could be expected in these domains with the use of CCM.

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